Subject: Pancreas Transplantation Procedures (Pancreas Alone, Simultaneous Pancreas and Kidney, Pancreas after Kidney and Pancreatic Islet Cell and Retransplantation)	Original Effective Date: 6/14/06
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DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (i.e., will be paid for by Molina) for a particular member. The member's benefit plan determines coverage. Each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their providers will need to consult the member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this Molina Clinical Policy (MCP)document and provide the directive for all Medicare members.[1 2 3]

DESCRIPTION OF PROCEDURE/SERVICE/PHARMACEUTICAL [61]

Pancreas transplantation is used to treat type 1 diabetes. The ultimate goal for pancreas transplantation is to improve the overall quality of life for the recipient. Transplantation, when successful, can eliminate the need for exogenous insulin, renal dialysis, and the associated primary and secondary complications that result from diabetes mellitus and renal failure (e.g., retinopathy, neuropathy, and vasculopathy). Nephropathy is a frequent major complication associated with both type 1 and type 2 diabetes and often ends in end-stage renal disease.

There are several types of Pancreas transplantation:

Pancreas Transplant Alone (PTA): Performed in labile diabetics with hypoglycemic unawareness and frequent ketoacidotic episodes without end stage renal disease. The goal is to limit or prevent complications that could cause permanent disability that may result from uncontrolled glucose levels (e.g., retinopathy, neuropathy, nephropathy, and vasculopathy).

Simultaneous pancreas kidney transplantation (SPK): Performed in Type I diabetes with end stage renal disease. Both organs come from the same living or deceased donor. The objectives are to restore glucose-regulated endogenous insulin secretion, arrest progression of complications, protect kidney damage from hyperglycemia and improve quality of life.

Pancreas after kidney transplantation (PAK): Performed in Type I diabetic patients with end stage renal disease. Two operations are required for this procedure. This is the treatment of choice for candidates with a living donor for a kidney transplant.

Allogeneic Pancreas Islet Cell Transplantation: Transplanting islet cells from a donor pancreas are infused into the patient's portal vein during the open procedure or postoperatively by a percutaneous approach.

Autologous Pancreas Islet cell autotransplantation: Transplanting islet cells from the patient's own resected pancreas and infused into the patient's portal vein during the open procedure or postoperatively by a percutaneous approach. Autologous islet cell transplantation as an adjunct to a total or near-total pancreatectomy is a technique used to salvage and transplant beta cells which may prevent complications of chronic diabetes in individuals with chronic pancreatitis.

POSITION STATEMENT RECOMMENDATION

All transplants require prior authorization from the Corporate Transplant Department. Solid organ transplant requests will be reviewed by the Corporate Senior Medical Director or qualified clinical designee. All other transplants will be by the Corporate Senior Medical Director or covering Medical Director. If the criteria are met using appropriate NCD and/or LCD guidelines, state regulations and/or MCP policies the Corporate Senior Medical Director's designee can approve the requested transplant.

Members must meet UNOS guidelines for transplantation and the diagnosis must be made by a *Specialist in the Disease* and or Transplant Surgeon.

Pre-Transplant Evaluation: Please see MCP-323 Pre-Transplant Evaluation for additional criteria and information.

Criteria for transplant evaluation include all of the following:

- ❑ History and physical examination
- ❑ Psychosocial evaluation and clearance:
  - No behavioral health disorder by history or psychosocial issues:
    - if history of behavioral health disorder, no severe psychosis or personality disorder
    - mood/anxiety disorder must be excluded or treated
    - member has understanding of surgical risk and post procedure compliance and follow-up required
  - Adequate family and social support
- ❑ EKG
- ❑ Chest x-ray
- ❑ Cardiac clearance is required
- ❑ Pulmonary clearance if evidence of pulmonary artery hypertension (PAH) or chronic pulmonary disease
- ❑ Lab studies:

- *Complete blood count, Kidney profile (blood urea nitrogen, creatinine), electrolytes, calcium, phosphorous, albumin, liver function tests, Coagulation profile (prothrombin time, and partial thromboplastin time)
- *Serologic screening for HIV, Epstein Barr virus (EBV), Hepatitis virus B (HBV), and Hepatitis C(HCV), cytomegalovirus (CMV), RPR and/or FTA:
  - If HIV positive all of the following are met:
    - CD4 count >200 cells/mm-3 for >6 months
    - HIV-1 RNA undetectable
    - On stable anti-retroviral therapy >3 months
    - No other complications from AIDS (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidioides mycosis, resistant fungal infections, Kaposi's sarcoma, or other neoplasm)
  - If abnormal serology need physician plan to address and/or treatment as indicated
- UDS (urine drug screen) if patient is current or gives a history of past drug abuse

❑ *Colonoscopy (if indicated or if patient is 50 ≥ older should have had an initial screening colonoscopy, after initial negative screening requires follow up colonoscopy every ten years) with complete workup and treatment of abnormal results as indicated

❑ *GYN examination with Pap smear for women ≥ 21 to ≤ 65 years of age or indicated (not indicated in women who have had a TAH or TVH) with in the last three year with complete workup and treatment of abnormal results as indicated

Within the last 12 months:

❑ Dental examination or oral exam showing good dentition and oral care or no abnormality on panorex or plan for treatment of problems pre or post-transplant

❑ *Mammogram (if indicated or > age 40) with complete workup and treatment of abnormal results as indicated

❑ *PSA if history of prostate cancer or previously elevated PSA with complete workup and treatment of abnormal results as indicated

***Participating Centers of Excellence may waive these criteria**

AND

Approval of a request for an Adult or Pediatric Pre-transplant Evaluation for **Kidney Transplant** include all of the following: [ALL]

❑ A comprehensive history and physical examination including: a current evaluation of the member's kidney disease (including GFR, dialysis history), past medical history, social history including drug/alcohol use and current smoking status, compliance with the prescribed plan of care, current BMI, current medications, any current lab or imaging results.

❑ Documentation of compliance with dialysis if the member is on dialysis. This should be provided from the dialysis center. Member description of dialysis compliance is not adequate to satisfy this criteria.

❑ Documentation of a hemoglobin A1c within target range for members with diabetes.

❑ For members with daily marijuana use: documentation of compliance with a physician prescribed and managed program of abstinence, and a reasonable expectation that the member will be abstinent from marijuana use during the transplant and immediate post-transplant time period. Daily marijuana use is an absolute contraindication for both transplant and pre-transplant evaluation unless there is a state mandate applicable for medical marijuana use and transplants, AND there is documentation of member compliance with a physician prescribed plan of care for prescribed marijuana use.

- ❑ For members with a BMI > 35, documentation of compliance with a physician prescribed and managed program of weight loss and a reasonable expectation that the member can achieve a BMI<=35 at the time of transplant.

For members who don't meet ALL of the above criteria, office visits with transplant providers (including transplant nephrologist, psychosocial providers, endocrinologist etc.) will be approved. This will facilitate generating the above, medically necessary documentation.

Transplant Criteria:
Pancreas Alone, Simultaneous pancreas-kidney transplantation and pancreas after kidney *Organ* transplantation from a donor may be ***considered medically necessary*** in adult members that have met all of the following criteria: [1-6 7-56 57] [ALL]

- ❑ All pre-transplant criteria are met; and
- ❑ Optimally managed for at least 12 months by an endocrinologist or pancreas transplant surgeon; and
- ❑ Documentation of insulin dependent Type 1 diabetes showing abnormal beta cell functioning: [1]
    - o Beta cell autoantibody positive; or
    - o Fasting C-peptide undetectable (e.g., than or equal to 110% of the laboratory's lower limit of normal and with a concurrently obtained fasting glucose<225mg/dl)**;** and
- ❑ Documented history of frequent medically uncontrolled labile (brittle) insulin dependent diabetes mellitus, with recurrent, acute and severe life threatening metabolic complications that have required previous hospitalization. (e.g., ketoacidosis, hypoglycemia or hyperglycemia attacks); [1] and
- ❑ Consistent failure of aggressive insulin management (e.g., insulin pump, adjusting amounts and frequencies of injected insulin, multiple daily blood glucose levels, and strict diet and exercise)
- ❑ A partial pancreas transplant from a living donor may be considered medically necessary as an acceptable alternative to cadaveric transplant for individuals who meet medical necessity criteria for pancreas transplant alone (PTA).
- ❑ Pancreas retransplantation after a failed primary pancreas transplant may be considered medically necessary for individuals who meet medical necessity criteria for pancreas transplant above.

AND

The requesting transplant recipient should not have any of the following **absolute contraindications**:

- ❑ Cardiac, pulmonary, and nervous system disease that cannot be corrected and is a prohibitive risk for surgery
- ❑ Malignant neoplasm with a high risk for reoccurrence, non-curable malignancy (excluding localized skin cancer)
- ❑ Systemic and/or uncontrolled infection
- ❑ AIDS (CD4 count < 200cells/mm3)
- ❑ Unwilling or unable to follow post-transplant regimen
    - o Documented history of non-compliance
    - o Inability to follow through with medication adherence or office follow-up
- ❑ Chronic illness with one year or less life expectancy
- ❑ Limited, irreversible rehabilitation potential
- ❑ Active untreated substance abuse issues, requires documentation supporting free from addiction for minimally 6 months if previous addiction was present
- ❑ No adequate social/family support

The requesting transplant recipient should be evaluated carefully and potentially treated if the following **relative contraindications** are present:

- ❑ Irreversible lung disease patients require consultation and clearance by a Pulmonologist prior to consideration of transplantation, this includes the following:
- ❑ Smoking, documentation supporting free from smoking for 6 months
- ❑ Active peptic ulcer disease
- ❑ Active gastroesophageal reflux disease
- ❑ CVA with long term impairment that is not amendable to rehabilitation or a patient with CVA/transient ischemic attack within past 6 months
- ❑ Obesity with body mass index of >30 kg/m^2 may increase surgical risk
- ❑ Chronic liver disease such as Hepatitis B/C/D, or cirrhosis which increases the risk of death from sepsis and hepatic failure requires consultation by a gastroenterologist or hepatologist
- ❑ Gall bladder disease requires ultrasound of the gall bladder with treatment prior to transplantation

AND

The following Pancreas transplantation specific requirements by transplantation type must also be met:

Pancreas Transplant Alone: [ALL]

- ❑ All of the above outlined main criteria are met AND all of the following criteria are present:
- ❑ The presence of minimally one secondary complication that has not progressed to end-organ failure such as proliferative diabetic retinopathy, neuropathy, gastroparesis, accelerated atherosclerosis; and
- ❑ Creatinine clearance glomerular filtration rate of ≥ 80ml/min, and
- ❑ Minimum proteinuria

Simultaneous pancreas-kidney transplant: [ALL]

- ❑ All of the above outlined main criteria are met AND all of the following criteria are present:
- ❑ The presence of minimally one secondary complication that has not progressed to end-organ failure such as proliferative diabetic retinopathy, neuropathy, gastroparesis, accelerated atherosclerosis; and
- ❑ The member has renal insufficiency with uremia or impending/ current end stage renal disease (ESRD) with poor renal function and one of the following: [ONE]
    - Currently on dialysis; or
    - Anticipated date of the member requiring dialysis would be within the next 6 months or demonstrates 50% or more decline in renal function in the past year

Pancreas after kidney Transplant: [ALL]

- ❑ All of the above outlined main criteria are met AND all of the following criteria are present:
- ❑ The presence of minimally one secondary complication that has not progressed to end-organ failure such as proliferative diabetic retinopathy, neuropathy, gastroparesis, accelerated atherosclerosis; and
- ❑ The member has a living organ donor for the kidney transplant procedure otherwise SPK should be considered; and
- ❑ Previously successful kidney transplant as evidenced by stable function of previous renal allograft; and

- ❑ Stable adequate kidney function as evidenced by creatinine clearance glomerular filtration rate of ≥ 45ml/min; and
- ❑ Minimum proteinuria

Autologous pancreatic islet cell transplantation: [40-56]

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

CONTINUATION OF THERAPY

When extension of a previously approved transplant authorization is requested, review using updated clinical information is appropriate.

- ❑ If Molina Healthcare has authorized prior requests for transplantation, the following information is required for medical review: [ALL]
  - Presence of no absolute contraindication as listed above;
  - History and physical within the last 12 months;
  - Kidney profile within the last 12 months;
  - Cardiac update if history of cardiac disease within two years (≥ 50 years of age);
  - Psychosocial evaluation or update within the last 12 months;
  - Per initial and updated history and physical, any other clinically indicated tests and/or scans as determined by transplant center physician or Molina Medical Director.

- ❑ If authorized prior requests for transplantation were obtained from another insurer, the following information is required for medical review: [ALL]
  - Authorization letter/documentation from previous insurer;
  - Presence of no absolute contraindication as listed above;
  - History and physical within the last 12 months;
  - Cardiac update if history of cardiac disease within two years (≥ 50 years of age);
  - Psychosocial evaluation or update within the last 12 months;
  - Per initial and updated history and physical, any other clinically indicated tests and/or scans as determined by transplant center physician or Molina Medical Director.

LIMITATIONS [1-6 57]

Any of the following conditions are considered experimental, investigational and unproven due to insufficient evidence in the peer reviewed published literature:

- ❑ Type II diabetes
- ❑ Allogeneic pancreas islet cell transplantation for any condition or xenotransplantation
- ❑ Bioartificial pancreas device

SUMMARY OF MEDICAL EVIDENCE [5-56]

The published medical evidence and outcomes for pancreas transplantation in the United States consists of registry data obtained from transplant centers that perform pancreas transplantation procedures and is available from the United

Network for Organ Sharing (UNOS) and Organ Procurement and Transplantation Network (OPTN) database. Registry data demonstrates graft survival rates and outcomes comparable to other organ transplants. [5]

Allogeneic pancreatic islet cell transplantation is considered investigational for all indications because the peer reviewed published evidence is insufficient to conclude that islet cell transplantation shows net benefits in type I diabetes or for any other indication. The U.S. Food and Drug Administration (FDA) have provided guidance to industry regarding investigational new drug development (IND) for allogeneic pancreatic islet cell products. However, to date, there is no FDA approved biologic license for allogeneic pancreatic islet cell products or for a bioartificial pancreas device.

Autologous islet cell transplantation for chronic pancreatitis [40-56]

Results of the peer reviewed published studies suggest that autologous islet cell transplantation may provide durable improvements in patient-reported pain, reduce narcotic use, provide adequate glycemic control and insulin independence in many patients, improve quality of life in patients with intractable and debilitating symptoms from chronic pancreatitis and improve survival with an acceptable level of mortality. Several systematic reviews of the literature on islet autotransplantation (IAT) after total pancreatectomy (TP) or partial pancreatectomy (PP) have been published. A summary of the most relevant publications is outlined below.

Kempeneers et al, (2019) identified 15 observational studies with a total of 1255 individuals who had chronic pancreatitis who underwent total pancreatectomy with islet autotransplant. The pooled 30-day mortality rate was 2% and the 1-year mortality rate was 4%. Four studies assessed the insulin-free rate at 1 year and the other 11 studies reported the insulin-free rate at last follow-up. In pooled analyses, the insulin-free rate at 1 year was 30% (95% confidence interval [CI], 20-43%) and at last follow-up the insulin-free event rate was 1.31 (95% CI, 0.74 to 2.31) per 10 person-years. In the 5 studies that reported this outcome, pain assessed by a 100-point visual analogue scale (VAS) decreased by a mean of 58 points (from a preoperative mean of 79 to a post-operative mean of 22). In 6 studies, the pooled 1-year opioid-free rate was 63% (95% CI, 46-77%). [42]

Wu et al (2015) performed a systematic review and meta-analysis evaluating outcomes of IAT after TP. A total of 12 studies with a total of 677 subjects were included. The insulin independent rate for IAT after TP at last follow-up was 3.72 per 100 person-years (95% CI, 1.00-6.44). The 30-day mortality was 2.1% (95% CI, 1.2-3.8%). The mortality at last follow-up was 1.09 per 100 person-years (95% CI, 0.21-1.97). Factors associated with incidence density of insulin independence in univariate meta-regression analyses included islet equivalents per kg body weight. [44]

Sutherland et al (2012) reported data from a single center series of 409 individuals with chronic pancreatitis who were treated between 1977 and 2011 with TP and IAT to relieve pain and preserve β-cell mass. Fifty-three of the 409 participants (13%) were children between the ages of 5 and 18 years. Post TP and IAT actuarial survival at 1 year was 96% in adults and 98% in children, and 5-year survival was 89% in adults and 98% in children. Overall, at 15 years post-surgery, two-thirds (66%) of the individuals were reported alive. Insulin independence at 3 years was noted in 30% of individuals (25% of adults and 55% of children), while partial function was reported in 33%. Surgical complications requiring reoperation during the initial admission occurred in a total of 15.9% of the individuals, with bleeding as the most common reason for reoperation experienced in 9.5%. There were a total of 5 (1.2%) in-hospital deaths, and 53 deaths following initial discharge with 3 of those deaths related to chronic pancreatitis disease processes. Insulin independence at 6 months was observed in 25% of individuals, 33% had partial islet function and less than one-fifth were dependent on insulin. Narcotic use for pain control declined after TP and IAT. The proportion of individuals requiring narcotics were, 91%, 61%, 54% and 51% at 3, 6, 12 and 24 months, respectively. A survey of integrated quality-of-life outcomes showed

that at 1 year of the 191 participants, 85% reported improvement compared to the prior year. The authors concluded TP alleviates pain caused by chronic pancreatitis and IAT can help to preserve glycemic control in most individuals. [43]

American Diabetes Association [57]

The 2020 & 2021 Standards of Medical Care in Diabetes by the American Diabetes Association recommends that islet autotransplantation should be considered for patients requiring total pancreatectomy for medically refractory chronic pancreatitis to prevent postsurgical diabetes. The standards state that "approximately one-third of patients undergoing total pancreatectomy with islet autotransplantation are insulin free 1 year postoperatively, and observational studies from different centers have demonstrated islet graft function up to a decade after the surgery in some patients. Both patient and disease factors should be carefully considered when deciding the indications and timing of this surgery. Surgeries should be performed in skilled facilities that have demonstrated expertise in islet autotransplantation."

CODING INFORMATION THE CODES LISTED IN THIS POLICY ARE FOR REFERENCE PURPOSES ONLY. LISTING OF A SERVICE OR DEVICE CODE IN THIS POLICY DOES NOT IMPLY THAT THE SERVICE DESCRIBED BY THIS CODE IS COVERED OR NON-COVERED. COVERAGE IS DETERMINED BY THE BENEFIT DOCUMENT. THIS LIST OF CODES MAY NOT BE ALL INCLUSIVE.

CPT	Description
0584T	Islet cell transplant, includes portal vein catheterization and infusion, including all imaging, including guidance, and radiological supervision and interpretation, when performed; percutaneous
0585T	Islet cell transplant, includes portal vein catheterization and infusion, including all imaging, including guidance, and radiological supervision and interpretation, when performed; laparoscopic
0586T	Islet cell transplant, includes portal vein catheterization and infusion, including all imaging, including guidance, and radiological supervision and interpretation, when performed; open
48160	Pancreatectomy, total or subtotal, with autologous transplantation of pancreas or pancreatic islet cells
48550	Donor pancreatectomy (including cold preservation), with or without duodenal segment for transplantation
48551	Backbench standard preparation of cadaver donor pancreas allograft prior to transplantation, including dissection of allograft from surrounding soft tissues, splenectomy, duodenotomy, ligation of bile duct, ligation of mesenteric vessels, and Y-graft arterial anastomoses from iliac artery to superior mesenteric artery and to splenic artery
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
50300	Donor nephrectomy (including cold preservation); from cadaver donor, unilateral or bilateral
50320	Donor nephrectomy (including cold preservation); open, from living donor
50323	Backbench standard preparation of cadaver donor renal allograft prior to transplantation, including dissection and removal of perinephric fat, diaphragmatic and retroperitoneal attachments, excision of adrenal gland, and preparation of ureter(s), renal vein(s), and renal artery(s), ligating branches, as necessary
50325	Backbench standard preparation of living donor renal allograft (open or laparoscopic) prior to transplantation, including dissection and removal of perinephric fat and preparation of ureter(s), renal vein(s), and renal artery(s), ligating branches, as necessary
50327	Backbench reconstruction of cadaver or living donor renal allograft prior to transplantation; venous anastomosis, each

50340	Recipient nephrectomy (separate procedure)
50360	Renal allotransplantation, implantation of graft; without recipient nephrectomy
50365	Renal allotransplantation, implantation of graft; with recipient nephrectomy
50370	Removal of transplanted renal allograft

HCPCS	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
S2102	Islet cell tissue transplant from pancreas; allogeneic
S2152	Solid organ(s), complete or segmental, single organ or combination of organs; deceased or living donor (s), procurement, transplantation, and related complications; including: drugs; supplies; hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services, and the number of days of pre and post-transplant care in the global definition

ICD-10 CM	Description: [For dates of service on or after 10/01/2015]
E10.10	Type 1 DM w/ketoacidosis w/o coma
E10.11	Type 1 DM w/ketoacidosisw/coma
E10.21	Type 1 DM w/diabetic nephropathy
E10.39	Type 1 DM w/oth diab ophthalmic comp
E10.40	Type 1 DM w/diab neuropathy unspec
E10.51	Type 1 DM w/diab periph angiopathy w/o gangrene
E10.65	Type 1 DM w/hyperglycemia
E10.69	Type 1 DM w/oth specified complication
E10.8	Type 1 DM w/unspec complications
K86.0-K86.1	Chronic pancreatitis
N18.5	Chronic kidney disease Stage V
N18.6	End stage renal disease
N18.9	Chronic kidney disease unspecified
Z99.2	Dependence on renal dialysis

RESOURCE REFERENCES

Government Agency

1. Centers for Medicare and Medicaid Services (CMS). National Coverage Determination for Pancreas Transplants (260.3). Accessed at: https://www.cms.gov/medicare-coverage-database/new-search/search.aspx
2. Centers for Medicare and Medicaid Services (CMS). National Coverage Determination for Islet Cell Transplantation in the context of a Clinical Trial NCD (260.3.1) Accessed at: https://www.cms.gov/medicare-coverage-database/new-search/search.aspx
3. Centers for Medicare and Medicaid Services (CMS) website. Decision memo for pancreas transplants. Accessed at: https://www.cms.gov/medicare-coverage-database/new-search/search.aspx
4. U.S. Food & Drug Administration. Guidance for Industry: considerations for allogeneic pancreatic islet cell products. September 2009. Available at: https://www.fda.gov

5. Organ Procurement and Transplantation Network (OPTN) and Scientific Registry of Transplant Recipients (SRTR). OPTN / SRTR Annual Data Report. Rockville, MD: Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation. Accessed at: http://www.srtr.org/
6. Organ Procurement and Transplantation Network (OPTN). Policy 11. Allocation of pancreas, kidney-pancreas, islets. Accessed at: http://optn.transplant.hrsa.gov/

Peer Reviewed Literature

7. Aguera ML, Navarro MD, Perez-Calderon R, et al. Simultaneous pancreas-kidney transplant: a single-center long-term outcome. J Nephrol. 2007;20(2):173-176
8. Arjona A, Matinez-Cecilia JF, uiz-Rabelo et al. One hundred one simultaneous pancreas-kidney transplantations: long term outcomes at a single center. (2009)Transplantation proceedings 41, 2463-2465
9. Bhagani, S., & Sweny, PI, Guidelines for kidney transplantation in patients with HIV disease. (2006). HIV Medicine. 7 (3):133-139.
10. Bhargava R, Mitsides N, Saif I et al. C-peptide and combined kidney pancreas transplantation. Nephrology Dialysis Transplantation, 2009: 1 of 4.
11. Biesenbach G, Biesenbach P. Bodlaj G et al. Impact of smoking on progression of vascular diabetes and patient survival in type-1 diabetic patients after simultaneous kidney-pancreas transplantation in a single centre. Tranplantation International 2008 Apr;21(4):357-63.
12. Cravedi P, van DM, Cattaneo I et al. Successes and disappointments with clinical islet transplantation. Advanced Exp Med Biology 2010;654.749-769.
13. Dean PG, Kudva YC,Stegall MD. Long-term benefits of pancreas transplantation. Current Opinion in Organ Transplantation. 2008;13:85-90.
14. Dieterle CD, Schmauss S, Arbogast H, et al. Pulmonary function in patients with type 1 diabetes before and after simultaneous pancreas and kidney transplantation. Transplantation. 2007;83(5):566-569
15. Fellmer PT, Pascher A, Kahl A et al. Influence of donor- and recipient specific factors on the postoperative course after combined pancreas-kidney transplantation. Langenbecks Archives Surgery 2010;395:19-25.
16. Fiorina P, Perseghin G, De Cobelli F et al. Altered kidney graft high-energy phosphate metabolism in kidney-transplanted end stage-renal disease type 1 diabetic patients: a cross sectional analysis of the effect of kidney alone and kidney-pancreas transplantation. Diabetes Care 2007;30:597-603.
17. Fridell JA, Mangus RS, Hollinger EF et al. The case for pancreas after kidney transplantation. Clinical Transplantation. 2009;23:447-453.
18. Gremizzi C, Vergani A, Paloschi V, Secchi A. Impact of pancreas transplantation on type 1 diabetes-related complications. Current Opinion in Organ Transplantation. 2010;15:119-123.
19. Gruessner AC. 2011 update on pancreas transplantation: comprehensive trend analysis of 25,000 cases followed up over the course of twenty-four years at the International Pancreas Registry (IPTR). Rev Diabet Stud 2011 Spring;8(1):6-16. Epub 2011 May 10.
20. Gruessner R, Sutherland DE, Kandaswamy R, Gruessner AC. Over 500 solitary pancreas transplants in nonuremic patients with brittle diabetes mellitus. Transplantation; January, 2008; 85(1):42-47.
21. Helou R. Should We Continue to Use the Cockcroft-Gault Formula? Nephron Clin Pract 2010;116:c172-c186 (DOI: 10.1159/000317197)
22. Hollinger EF, Powelson JA, Mangus RS et al. Immediate retranplantation for pancreas allograft thrombosis. American Journal of Tranplantation. 2009;9:740-746.
23. Jaeckel E, Lehner F. Pancreas and islet transplantation. 2009;50(5):536-549.
24. Kleinclauss F, Fauda M, Sutherland DE, et al. Pancreas after living donor kidney transplants in diabetic patients: impact on long-term kidney graft function. Clinical Transplant 2009 Aug-ept;23(4):435-436.
25. Linetsky E, Ricordi C. Regulatory challenges in manufacturing of pancreatic islets. Transplant Proc. 2008 Mar;40(2):424-6.

26. Lipshutz GS, Wilkinson AH, Pancreas-kidney and pancreas transplantation for the treatment of diabetes mellitus. Endocrinology and metabolism clinics of North America. 2007;36:1015-1018.
27. Morath C, chimed B, Mehrabi A et al. Simultaneous pancreas-kidney transplantation in type 1 diabetes. Clinical Transplant 2009;23 Suppl 21115-120
28. Morath C, Zeier M, Dohler B et al. Metabolic control improves long-term renal allograft and patient survival in type 1 diabetes, Journal American Society Nephrology 2008:19:1557-63.
29. Odorico JS, Voss B, Munoz Del RA et al. Kidney function after solitary pancreas transplantation. Transplant Procedure 2008;40(2):513-515.
30. Pavlakis M, Khwaja K, Mandlebrot D et al. Renal allograft failure predictors after PAK transplantation: results from the New England Collaborative Association of Pancreas Programs. Transplantation 2010;89:1347-1353
31. Sampaio, MS, Reddy P, Kuo HT et al. Obesity was associated with inferior outcomes in simultaneous pancreas kidney transplant. Transplantation 2010; 89: 1117-1125.
32. Scalea JR, Butler CC, Munivenkatappa RB et al. Pancreas transplant alone as an independent risk factor for the development of renal failure: A retrospective study. Transplantation December, 2008;86(12):1789-1794.
33. Seal J, Selzner M, Laurence J, et al. Outcomes of Pancreas Retransplantation After Simultaneous Kidney-Pancreas Transplantation Are Comparable to Pancreas After Kidney Transplantation Alone. Transplantation. 2014 Aug;21.
34. Siskind E, Maloney C, Akerman M, et al. An analysis of pancreas transplantation outcomes based on age groupings--an update of the UNOS database. Clin Transplant. Sep 2014;28(9):990-994.
35. Shah, AP, Mangus, RS, Powelson, JA, et al. Impact of recipient age on whole organ pancreas transplantation. Clin Transplant. 2013 Jan-Feb;27(1):E49-55. PMID: 23228216
36. Afaneh, C, Rich, BS, Aull, MJ, Hartono, C, Leeser, DB, Kapur, S. Pancreas transplantation: does age increase morbidity? J Transplant. 2011;2011:596801. PMID: 21766007
37. Schenker, P, Vonend, O, Kruger, B, et al. Long-term results of pancreas transplantation in patients older than 50 years. Transpl Int. 2011 Feb;24(2):136-42. PMID: 21039944

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38. Lablanche S, Vantyghem MC, Kessler L et al. Islet transplantation versus insulin therapy in patients with type 1 diabetes with severe hypoglycaemia or poorly controlled glycaemia after kidney transplantation (TRIMECO): a multicentre, randomised controlled trial. Lancet Diabetes Endocrinol. 2018; 6(7):527-537.
39. Maffi P, Nano R, Monti P et al. Islet allotransplantation in the bone marrow of patients with type 1 diabetes: a pilot randomized trial. Transplantation. 2018; 103(4): 839-851
40. Bellin MD, Beilman GJ, Dunn TB, et al. Sitagliptin treatment after total pancreatectomy with islet autotransplantation: A randomized, placebo-controlled study. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons. 2017;17(2):443-450.
41. Bramis K, Gordon-Weeks AN, Friend PJ, et al. Systematic review of total pancreatectomy and islet autotransplantation for chronic pancreatitis. Br J Surg. 2012; 99(6):761-766.
42. Colling KP, Bellin MD, Schwarzenberg SJ, et al. Total pancreatectomy with intraportal islet autotransplantation as a treatment of chronic pancreatitis in patients with cftr mutations. Pancreas. 2018;47(2):238-244.
43. Dong M, Parsaik AK, Erwin PJ, et al. Systematic review and meta-analysis: islet autotransplantation after pancreatectomy for minimizing diabetes. Clin Endocrinol (Oxf). 2011; 75(6):771-779.
44. Fazlalizadeh R, Moghadamyeghaneh Z, Demirjian AN, et al. Total pancreatectomy and islet autotransplantation: A decade nationwide analysis. World journal of transplantation. 2016;6(1):233-238.
45. Kempeneers MA, Scholten L, Verkade CR, et al. Efficacy of total pancreatectomy with islet autotransplantation on opioid and insulin requirement in painful chronic pancreatitis: A systematic review and meta-analysis. Surgery. 2019; 166(3):263-270.
46. Kesseli SJ, Wagar M, Jung MK, et al. Long-term glycemic control in adult patients undergoing remote vs. Local total pancreatectomy with islet autotransplantation. The American journal of gastroenterology. 2017;112(4):643-649.

47. Kizilgul M, Wilhelm JJ, Beilman GJ, et al. Effect of intrapancreatic fat on diabetes outcomes after total pancreatectomy with islet autotransplantation. Journal of diabetes. 2018;10(4):286-295.
48. Lane A, Hodges JS, Ptacek P, et al. Low prevalence of diabetes distress following total pancreatectomy with islet autotransplantation. Clinical transplantation. 2018;32(5):e13237.
49. Morgan KA, Lancaster WP, Owczarski SM, Wang H, Borckardt J, Adams DB. Patient selection for total pancreatectomy with islet autotransplantation in the surgical management of chronic pancreatitis. Journal of the American College of Surgeons. 2018;226(4):446-451.
50. Shahbazov R, Naziruddin B, Salam O, et al. The impact of surgical complications on the outcome of total pancreatectomy with islet autotransplantation. American journal of surgery. 2020;219(1):99-105.
51. Sutherland DE, Radosevich DM, Bellin MD, et al. Total pancreatectomy and islet autotransplantation for chronic pancreatitis. J Am Coll Surg. 2012; 214(4):409-424.
52. Wu Q, Zhang M, Qin Y, et al. Systematic review and meta-analysis of islet autotransplantation after total pancreatectomy in chronic pancreatitis patients. Endocr J. 2015; 62(3):227-234.
53. Wilson GC, Sutton JM, Abbott DE, et al. Long-term outcomes after total pancreatectomy and islet cell autotransplantation: is it a durable operation? Ann Surg. 2014;260(4):659-667.
54. Wilson GC, Sutton JM, Smith MT, et al. Completion pancreatectomy and islet cell autotransplantation as salvage therapy for patients failing previous operative interventions for chronic pancreatitis. Surgery. 2015b;158(4):872-880.
55. Wilson GC, Sutton JM, Smith MT, et al. Total pancreatectomy with islet cell autotransplantation as the initial treatment for minimal-change chronic pancreatitis. HPB (Oxford). 2015a;17(3):232-238.
56. Zhang YJ, Duan DD, Yuan H. Efficacy and safety of islet autotransplantation after total pancreatectomy in chronic pancreatitis: A systematic review and meta-analysis including 17 studies. Clinics and research in hepatology and gastroenterology. 2019.

Professional Society Guidelines

57. American Diabetes Association (ADA): Accessed at: https://diabetesjournals.org
    - Position Statement. Pancreas and Islet Transplantation in Type 1 Diabetes. Diabetes Care April 2006 vol. 29 no. 4 935.
    - American Diabetes Association Standards of Medical Care in Diabetes 2020-2021. Position Statements. 4. Comprehensive Medical Evaluation and Assessment of Comorbidities.
58. Piper M, Seidenfeld J, Aronson N. Islet Transplantation in Patients with Type 1 Diabetes Mellitus. Summary, Evidence Report/Technology Assessment: Number 98. AHRQ Publication Number 04-E017-1, July 2004. Agency for Healthcare Research and Quality, Rockville, MD. Available at: http://www.ahrq.gov/clinic/epcsums/isletsum.htm.
59. Steinman TI, Becker BN, et al.; Clinical Practice Committee, American Society of Transplantation. Guidelines for the referral and management of patients eligible for solid organ transplantation. Transplantation. 2001 May 15;71(9):1189-204.
60. Health Quality Ontario. Pancreas islet transplantation for patients with type 1 diabetes mellitus: A clinical evidence review. Ont Health Technol Assess Ser. 2015; 15(16):1-84.

Hayes

61. Hayes a Division of TractManager Health Technology Assessment. Winfred Hayes Inc., Lansdale, PA
    - Pancreas Transplantation Alone (PTA). Lansdale, PA: Hayes, Inc. February, 2006. Updated March, 2010 and archived March, 2011
    - Simultaneous Pancreas-Kidney (SPK) Transplantation in Diabetic Patients. January, 2008. Updated Feb, 2017, archived April 2018.
    - Pancreas-After-Kidney (PAK) Transplantation in Diabetic Patients. June, 2006. Updated June, 2010 and archived July, 2011

- Islet Cell Transplantation for the Treatment of Type 1 Diabetes. August, 2004. Updated July, 2009 and archived Sept, 2009
- Total Pancreatectomy with Islet Autotransplantation for Chronic Pancreatitis. Dec 2015. Updated Jan, 2020 and archived Jan, 2021

62. Hayes Search & Summary: Winfred Hayes Inc., Lansdale, PA
    - Pancreas Transplant Alone (PTA) for Pediatric Patients with Diabetes Mellitus, Feb 2017. Archived March, 2018.
    - Simultaneous Pancreas and Kidney Transplant (SPK) for Pediatric Patients with Diabetes Mellitus, Feb. 2017, archived March 2018.
    - Pancreas after Kidney Transplant (PAK) for Pediatric Patients with Diabetes Mellitus, Feb 2017. Archived March, 2018.

Other Resources

63. Dynamed. Diabetes Mellitus Type 1, pancreas transplant. Ipswich, MA: EBSCO Publishing. 1998-2021.
64. UpToDate: [website]. Waltham, MA: Walters Kluwer Health; 2021.
    - Aly ZA, Bloom RD, Murphy B, Post TW. Renal function and nonrenal solid organ transplantation.
    - Robertson RP, Brennan DC, et al. Patient selection for and immunologic issues relating to kidney-pancreas transplantation in diabetes mellitus.
    - Robertson RP, Nathan DM, Mulder JE. Pancreas and islet transplantation in diabetes mellitus.
    - Alhamad T, Stratta RJ. Pancreas-kidney transplantation in diabetes mellitus: Patient selection and pretransplant evaluation.
65. Advanced Medical Review (AMR): Policy reviewed by MD board certified in Surgery, Transplant. 8/30/12, & 1/21/20
66. Collaborative Islet Transplant Registry (CITR). Available at: http://citregistry.org/.
67. National Institute of Diabetes and Digestive and Kidney Diseases. Pancreatic Islet Transplantation. Available at: https://www.niddk.nih.gov/health-information/diabetes/overview/insulin-medicines-treatments/pancreatic-islet-transplantation.

REVIEW/REVISION HISTORY

6/14/06: New Policy
8/28/07: Policy reviewed by a Board certified Endocrinologist and Board Certified Pancreas Transplant Surgeon. Pancreas transplant alone criteria was added.
8/25/10: Policy reviewed and the changes include: Some of the contraindications were moved from absolute to the relative contraindications section. The pancreas transplant alone (PTA) section has a new requirement of glomerular filtration rate (GFR) of > 80ml/min and minimal proteinuria. This was based upon recent studies that demonstrated improved outcomes in patients meeting these criteria. The document was reviewed by an AMR physician Board certified in General Surgery General, and Transplant Surgery.
10/31/12: Policy reviewed and the changes include updated criteria for pre-transplant evaluation and HIV and AIDS patients. Summary of medical evidence section was updated.
5/26/15: This policy was reviewed and was updated with new pretransplant criteria and one new exclusion for bioartificial pancreas devices. The medical evidence section was condensed.
12/14/16, 6/22/17: Policy reviewed, no changes
9/13/18 & 9/18/19: Policy reviewed, no changes to criteria, updated references
4/23/20: Policy reviewed and updated with medically necessary criteria for autologous pancreatic islet cell transplantation when used as an adjunct to a total or near total pancreatectomy in patients with chronic pancreatitis. Updated references,

guidelines and added three new 2020 CPT codes (0584T, 0585T, 0586T) and one new ICD-10 code (K86.0-K86.1) for chronic pancreatitis.
6/9/21: Policy reviewed, no changes. Updated references. Coding reviewed by K. O'Brien, coder. Added CPT codes: 48551, 48552, 50323, 50325, 50327.