Cigna Medical Coverage Policy

Subject **Kidney Transplantation, Pancreas-Kidney Transplantation, and Pancreas Transplantation Alone**

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Coverage Policy

Note: Selected candidates may be eligible for multi-organ transplantation. In each case, the candidate should meet all of the criteria for selection for the individual transplant being considered.

Kidney and Simultaneous Pancreas-Kidney Transplantation

Cigna covers EITHER of the following procedures as medically necessary:

- kidney transplantation for an individual with end-stage renal disease
- simultaneous pancreas-kidney transplantation for an individual with type I diabetes mellitus and impending or established end stage renal disease

when EITHER of the following criteria is met:

- glomerular filtration rate (GFR) of < 23 mL/min/1.73m^2
- GFR ≥ 23 but < 29 mL/min/1.73m^2 with evidence of uremia, including ANY of the following:
  - anemia of chronic disease
  - nausea, vomiting or anorexia
  - pericarditis or uremic serositis
  - uremic encephalopathy
  - metabolic acidosis (HCO3 < 15 meq/l)
  - persistent hyperkalemia (K^+ > 6.0 meq/l)

- pulmonary edema or congestive heart failure refractory to diuretics
- incapacitating peripheral edema refractory to diuretics
- peripheral or autonomic neuropathy
- uncontrollable hypertension
- requiring dialysis or meeting criteria for dialysis
- pediatric only: growth failure as compared to children of same age and gender (weight is < 3rd to 5th percentile, height is > 2 standard deviations below mean; or weight crosses two major percentiles downward, utilizing 90th, 75th, 50th, 10th and 5th)

Pancreas-After-Kidney Transplantation

Cigna covers pancreas-after-kidney transplantation (PAK) as medically necessary for an individual with type I diabetes mellitus.

Pancreas Transplantation Alone

Cigna covers pancreas transplantation alone (PTA) as medically necessary for an individual with type I diabetes mellitus, which despite maximal medical management and adherence to treatment recommendations, is poorly controlled as manifested by the presence of BOTH of the following:

- history of frequent, acute and severe metabolic complications (e.g., hypoglycemia, hyperglycemia, ketoacidosis) of such severity that requires medical attention
- failure of insulin-based management to prevent acute complications

Not Covered

Cigna does not cover kidney, pancreas, or pancreas-kidney transplantation for an individual with ANY of the following contraindications to transplant surgery because it is considered not medically necessary (this list may not be all-inclusive):

- malignancy that is expected to significantly limit future survival
- persistent, recurrent or unsuccessfully treated major or systemic extra-renal infections
- systemic illness or comorbidities that would be expected to substantially negatively impact the successful completion and/or outcome of transplant surgery
- a pattern of demonstrated patient noncompliance which would place a transplanted organ at serious risk of failure
- human immunodeficiency virus (HIV) disease unless ALL of the following are noted:
  - CD4 count greater than 200 cells/mm3
  - HIV-1 ribonucleic acid (RNA) undetectable
  - Stable anti-retroviral therapy for more than three months
  - Absence of serious complications associated with HIV disease (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidioidomycosis, or resistant fungal infections; or Kaposi's sarcoma or other neoplasm)

Cigna does not cover EITHER of the following because each is considered experimental, investigational or unproven (this list may not be all inclusive):

- living donor pancreas transplantation (i.e., partial pancreas transplantation, segmental pancreas transplantation)
- bioartificial pancreas device

General Background

End-stage renal disease (ESRD) occurs when the kidneys are no longer able to function at a level that is necessary for day-to-day life. ESRD almost always follows chronic kidney failure, which may exist for 10–20

years or more before progression to end-stage renal disease (ESRD). The most common cause of ESRD in the U.S. is diabetes mellitus. Other diseases that may lead to ESRD include hypertension, polycystic kidneys, nephrosclerosis, chronic pyelonephritis, glomerulonephritis, kidney stones, renal cell carcinoma and Wilm's tumor.

Glomerular filtration rate (GFR) is considered the best measure of kidney function. While the lower limit of normal GFR varies with age, a GFR level below 60 mL per minute per 1.73m^2 represents loss of one half or more of the adult level of normal kidney function. A GFR of <30 mL/min/1.73 m^2 is considered to be abnormal in all ages other than neonates.

Kidney failure, (i.e., chronic kidney disease [CKD] stage 5) is defined as either a GFR below 15 mL per minute per 1.73 m^2 which, in most cases is accompanied by signs and symptoms of uremia, or a need to start kidney replacement therapy (i.e., dialysis or transplantation) for the treatment of complications of decreased GFR (Johnson, et al. 2004; Levey, et al. 2003). Authors recommend patients be referred to a nephrologist for renal replacement therapy when the GFR is <30 mL/min/1.73 m^2 (i.e., stage 4) (Eknoyan and Levin, 2002; Bolton, 2003). Patients with advanced CKD (Kidney Disease Outcomes Quality Initiative [K/DOQI™] CKD Stages 4 and 5) have a high propensity for progression to ESRD in a relatively short period of time with well-known multiple comorbid conditions and poor outcomes (Bolton, 2003).

Kidney Transplantation
Kidney transplantation is the grafting of a kidney from either a living or deceased (i.e., cadaver) donor. Both pediatric and adult kidney transplant recipients have increased survival compared to patients who remain on dialysis. The transplant procedure can be performed by open surgical approach or laparoscopically. The use of laparoscopic nephrectomy has reduced the length of hospital stay, pain, and recovery time for donors while having no effect on the quality of the donated organ.

Kidney transplantation should be timed to occur as close as possible to when the recipient would be expected to require dialysis; however, transplantation should be delayed in patients who may regain kidney function (e.g., malignant hypertension, severe, acute tubular necrosis). Transplantation performed prior to the need for dialysis is called preemptive transplantation. It confers a survival advantage to the recipient and is more common for recipients of living-donor kidneys. Preemptive kidney transplant has been shown to provide better outcomes compared to transplant after any period of time on dialysis; however, because of the shortage of donors, preemptive transplantation may not be possible.

Living-donor kidneys account for approximately 40% of all kidney transplants (Markmann, et al., 2007). Living donors can be related or unrelated to the recipient. Living kidney donation eliminates the recipient's need for waiting time on a national waiting list, are often more successful, and can add psychological benefits to both donor and recipient. Nonetheless, the benefit to the recipient of a live-donor organ must outweigh the risks to the donor. In the absence of a living donor, many transplanted kidneys come from deceased (i.e., cadaver) organ donors. One, three-, and five-year graft survival rates for cadaver kidney transplantation are 91.9%, 82.4%, and 72.0%, respectively (OPTN, 1997-2004, based on OPTN data as of Aug 9, 2013).

Donor Matching
In the event that an ABO-identical or minor mismatch donor is unavailable, the use of an ABO mismatched donor may be the best option for some kidney transplantation candidates. Recent studies have demonstrated that an ABO mismatched living donor transplant may result in survival rates close to those achieved with compatible grafts, although recipients with high anti-blood group titers before plasmapheresis have been reported to have higher rates of humeral rejection and early graft loss (Shimmura, et al., 2000; Sonnenday, et al., 2004; Stegall, et al., 2004; Kaihara, et al., 2005).

Extended Criteria Donor Kidney
In an effort to address the shortage of kidneys available for transplantation, the kidney allocation algorithm was modified in October 2002 to expedite the distribution of kidneys with less favorable donor characteristics, known as extended criteria donor (ECD) kidneys. This includes kidneys from donors over the age of 60 or ages 50–60 with two or all three of the following criteria:

- pre-donation serum creatinine greater than 1.5 mg/dL (milligrams per deciliter)
- stroke as cause of death

- hypertension

Graft and patient survival for ECD kidney recipients are not as favorable as those for non-ECD kidney recipients, and both of these groups have lower survival than patients who received living-donor kidneys.

Kidney Allocation System (KAS): A new kidney allocation system (KAS) was developed by the Organ Procurement and Transplantation Network (OPTN) Kidney Transplantation Committee in response to higher than necessary discard rates of kidneys, variability in access to transplants for candidates who are harder to match due to biologic reasons, and a matching system that results in unrealized life years and high re-transplantation rates. According to the OPTN (2014), the new KAS is expected to be in effect by the end of 2014.

The KAS includes the following changes:

- replacement of the current kidney donor quality metric with the Kidney Donor Profile Index (KDPI)
- adult transplant candidates will receive an Expected Post Transplant Survival (EPTS) score
- allocation rules will use the KDPI for donors and the EPTS score for longevity matching between donors and recipients.
- sensitized candidates will be given increased priority through a sliding scale points system for calculated panel reactive antibodies (CPRA) and regional and national sharing for very highly sensitized candidates
- pre-registration dialysis time will be included in a candidate's waiting time.
- increased access to donor kidneys for blood type B candidates
- elimination of the payback system
- other variances are being eliminated with implementation of the new system.

Retransplantation
In general, retransplantation is considered by some to be a controversial procedure, in part due to ethical concerns over the limited supply of organs. A wide range of donor, recipient and other transplant-related factors can influence graft survival. In the event of renal graft failure, renal replacement therapy consists of either dialysis or retransplantation. Although allograft survival is considered good, it is considerably less compared to the primary transplant (Ahmed, et al., 2008). Candidates awaiting kidney retransplant are often allosensitized and may be less likely to receive a transplant than primary candidates. As a result, some transplant centers have developed ongoing efforts involving desensitization protocols to prevent antibody-mediated acute rejection. Although desensitization protocols may be considered for deceased donor kidney, protocols are generally attempted with living donation so that antibody response against donor tissue can be monitored; patients proceed to transplant surgery only if antibody levels are low. Authors contend that desensitizing highly sensitive patients improves clinical outcomes (short-term patient and graft survival) however acute antibody-mediated rejection is a barrier in 20-30% of patients and there is no consensus regarding which protocol is ideal (Akalin, 2009).

Pancreas-Kidney Transplantation and Pancreas Transplantation Alone
The pancreas is a gland with both exocrine and endocrine function. The exocrine function is essential for protein and fat digestion. The endocrine function involves the production of insulin, glucagons, and somatostatin with subsequent release of these hormones into the blood stream. Insulin acts to decrease blood sugar levels, glucagon acts to increase the blood sugar and somatostatin interacts with growth hormone, insulin and glucagons. Lack of insulin production results in diabetes mellitus.

The standard treatment for control of blood sugar levels in type I diabetes mellitus (DM), is the use of exogenous insulin; however, this does not entirely restore normal glucose metabolism. Beta-cell replacement by organ (pancreas) or by islet cell is the only method of treatment that will restore normal glucose metabolism in individuals who are insulin-dependent.

Pancreas transplantation eliminates the need for exogenous insulin, daily glucose monitoring and many dietary restrictions imposed by diabetes. Additional benefits of pancreas transplantation include the elimination of life-threatening risks of hypoglycemic unawareness and prevention and reversal of diabetic nephropathy (Bloom, et al., 2005). Replacement by organ (pancreas transplantation) may be performed simultaneously with kidney

transplants (i.e., simultaneous pancreas kidney [SPK]) or after a kidney transplant (i.e., pancreas after kidney [PAK]) in individuals who are uremic, or alone in individuals who are nonuremic (i.e., pancreas transplant alone [PTA]). The donated kidney can be from a living donor or a cadaveric donor. The donated pancreas is usually a whole pancreas from a cadaver, but has been performed using a segment of pancreas from a living donor.

Type I Diabetes Mellitus (DM)
Type I diabetes mellitus, also known as insulin-dependent diabetes mellitus [IDDM] and juvenile-onset diabetes, accounts for only 5-10% of those with diabetes and typically occurs in childhood or adolescence, although it may occur at any age, even in the eighth or ninth decades of life (ADA, 2013). It results from a cellular-mediated autoimmune destruction of the beta cells (β-cells) located in the islets of Langerhans in the pancreas. The primary purpose of β-cells is to store and release insulin. In type I DM the body's immune system attacks and destroys the β-cells. The rate of β-cell destruction varies being rapid in infants and children and slow in adults. Destruction of these cells leads to progressive insulin deficiency and hyperglycemia. Individuals with type I DM require insulin therapy for life.

Markers of the immune destruction of the β-cell include islet cell autoantibodies, autoantibodies to insulin, autoantibodies to glutamic acid decarboxylase (GAD65), and autoantibodies to several tyrosine phosphatases. At least one, and usually more of these autoantibodies are present in 85–90% of individuals when fasting hyperglycemia is initially detected. Autoantibody testing is performed to help distinguish type I from type 2 DM. The presence of insulin antibodies is common in individuals who are taking insulin and is not an indicator of the type of diabetes (ADA, 2013; Bylund and Nakamura, 2011; Eisenbarth and Buse 2011; Towns and Pietropaolo, 2011).

According to the ADA (2013), ketoacidosis may be the first manifestation of the disease, especially in children and adolescents. In others, a modest fasting hyperglycemia may rapidly change to severe hyperglycemia and/or ketoacidosis in the presence of infection or other stressors. Adults particularly may retain residual β-cell function sufficient to prevent ketoacidosis for many years although they may eventually become dependent on insulin for survival and are at risk for ketoacidosis. Little or no insulin production is manifested by low or undetectable levels of plasma C-peptide (ADA, 2013). C-peptide is a polypeptide of 31 amino acids and a byproduct of insulin production. The level of C-peptide in the body reflects the amount of insulin being produced and can be measured to determine if a patient has type I or type 2 diabetes. An individual with type I DM whose pancreas does not make insulin has a low level of C-peptide.

Type II Diabetes Mellitus (DM)
Pancreas transplant is not typically used for the treatment of individuals with type II DM. In contrast to persons with type 1 DM, individuals who have type II DM produce some insulin; however, for unknown reasons, the body is unable to use it effectively. While in general there is no simple laboratory test to distinguish between type I and type II DM, C-peptide levels are often used to verify insulinopenia, in combination with a documented clinical exam and/or insulin sensitivity and resistance testing. Clearly identifying individuals with type II DM who are candidates for pancreas transplant is challenging; C-peptide levels increase in the presence of renal disease and there is limited information regarding C-peptide levels for defining the type of diabetes in study subjects with ESRD.

Typically, a person with type II DM has a normal C-peptide level. A fasting C-peptide level that is ≤ 110% of the lower limit of normal of the laboratory's measurement method and a concurrently obtained fasting glucose of ≤ 225 mg/dL is indicative of insulinopenic type II DM. For example, if the laboratory normal C-peptide range was 0.78–1.89 nanograms/milliliter (ng/mL) then the individual with insulopenic type II DM without renal insufficiency would have a value of ≤ 0.86 ng/mL and with renal sufficiency would have a value of ≤1.56 ng/mL. Insulopenia is diagnosed in less than 5% of type II DM (NLM, 2014; Centers for Medicare and Medicaid [CMS], 2005; CMS, 2001).

Despite these challenges, some authors have proposed pancreas transplantation to achieve insulin independence in persons with type II DM demonstrating insulinopenia, and have shown encouraging results (Light and Barhyte, 2005; Nath, et al., 2005). However, evidence in the peer-reviewed, published scientific literature supporting the ability of pancreas transplantation to achieve insulin independence in this subset of individuals has not been consistently demonstrated and is not a proven standard of care. Pancreas transplantation as an alternative treatment for individuals with type II DM and insulinopenia remains controversial.

Living Donor Pancreas Transplantation
Both the American Diabetes Association and the United Network for Organ Sharing (UNOS) recognize and provide information regarding living donor pancreas transplantation. Living donor pancreas transplantation has been performed in a few centers, including those outside the United States; however it is not considered widespread in clinical practice. In many cases, the living pancreas donor is a relative of the recipient. In the United States living donor pancreas transplantation has been largely studied at one center, the University of Minnesota. Barr et al. (2006) reported that at the University of Minnesota there were 130 live donor pancreas transplants between 1977 and 2005; 20 PTA and PAK live donor grafts were functioning between 10 and 20 years following transplant; 3 living donor SPK were functioning greater than 10 years. More limited data is available from the University of Chicago where the procedure is performed less frequently.

Living donor pancreas transplantation is a highly specialized procedure; there is a higher technical failure rate and as potential for complications associated with the donor operation (Gruessner, et al., 2001). During the procedure for living-donor pancreas transplant, a hemipancreatectomy is performed on the living donor (either open or laparoscopically) and then implanted as a segment into a recipient with diabetes mellitus. As a result, there is potential risk for development of diabetes in the donor and ongoing assessment is important. Nevertheless, compared to a matched deceased organ, the use of a living donor pancreas reduces wait time, offers enhanced immunologic compatibility, and decreases cold ischemic injury.

In 2003 ECRI conducted a health technology assessment to evaluate living donor pancreas transplantation. At the time of the review, the evidence consisted of published case series from two centers: the University of Minnesota and the University of Illinois at Chicago. After reviewing the evidence ECRI concluded that the effectiveness of living donor simultaneous pancreas kidney (SPK) transplantation in terms of recipient and graft survival rates appeared to be comparable to, and perhaps slightly better than, cadaveric transplantation results. There was no difference in recipient morbidity between living donor and cadaveric transplant. There was no reported mortality among donors and short-term morbidity appeared to be low, however they reported long-term consequences for donors were unknown.

The evidence for living donor pancreas transplantation is primarily in the form of few retrospective case series, case reports, and patient-registry data (Troppman, et al., 1996; Gruessner, et al. 1997; Humar, et al., 1997; Tan, et al., 2005; Horgan, et al., 2007). Measured outcomes include graft and patient survival and as well as adverse events. A small number of case studies have suggested a patient survival rate of up to 85-90% at five years after receiving a living-related donor pancreas transplant (Gruessner, et al., 2001; Humar, et al., 1997). Evidence regarding the long-term effects of transplant on glycemic control or the impact on secondary diabetic complications is limited. Additionally, the peer-reviewed scientific evidence suggests living donor pancreas grafts are more prone to arterial and venous thrombosis and infection, although graft rejection is lower compared to cadaveric transplant. Long-term clinical outcomes have not been reported and it has not been clearly established that living donor pancreas transplantation reverses complications associated with diabetes. However, in the short-term, there is limited evidence supporting normalizing insulin production for selected individuals.

Patient selection criteria for living donor pancreas transplantation have not been clearly defined in the medical literature. It has been suggested that the best recipients are those with high panel-reactive antibody concentrations who are likely to have a long wait for a deceased donor, but have a crossmatch negative live donor whose beta cell reserve is excellent (White, et al., 2009). According to this same group of authors, exclusion criteria generally include diabetes in first degree relatives, gestational diabetes, body mass index greater than 27 $kg/m^{2,}$ hemoglobin A_{1c} greater than 6% and age over 50 years.

The risks of complications to the live kidney donor are not the same as the risks for being a live liver, lung, intestine or pancreas donor. Reynoso et al. (2009) reported that although there have been no reports of living donor morbidity from the surgical procedure, a reluctance to use living donors for pancreas transplant is based on the anatomy of the pancreas as an unpaired organ and the risk of serious organ-specific complications, such as pancreatitis, leak and pseudocyst. Furthermore, possible deterioration of glucose metabolism as a result of the hemipancreatectomy is a lifelong concern to the donor.

Simultaneous Pancreas-Kidney (SPK)/Pancreas-after-Kidney (PAK)

Kidney failure is a major complication of DM and, as a result, most potential pancreas transplant recipients are also uremic. Due to the poor five-year survival rate of individuals with DM who are on dialysis, kidney transplantation is the treatment of choice for individuals with DM who have ESRD and are on dialysis.

Individuals with type 1 DM and impending or established ESRD who have minimal or limited secondary complications of DM are considered optimal candidates for kidney transplantation (Pirsch and Stratta, 2001). Increasingly, pancreas transplantation is being offered to individuals who require kidney transplantation or who had a previously successful kidney transplant. SPK is performed to correct complications of type 1 DM and renal failure with reliance on dialysis. In individuals with type 1 DM who have had a successful kidney transplantation to correct previous uremia, PAK is performed to improve quality of life by: 1) eliminating the need for exogenous insulin and its associated difficulty controlling glucose levels; and 2) to limit secondary diabetic complications, including retinopathy, neuropathy, nephropathy, and vasculopathy. There is some concern regarding the appropriateness of pancreas transplantation because of the increased morbidity associated with the procedure and the lack of controlled trials that demonstrate a significant benefit on secondary complications of DM. Despite these concerns, pancreas transplantation is an appropriate option for individuals with DM who have complications, since it can enhance quality of life and is the single most effective method of achieving tight glucose control (Pirsch and Stratta, 2001).

Evidence in the scientific published literature supports SPK and PAK transplantation as an appropriate therapeutic intervention for individuals with type I DM who require or have previously had a kidney transplant (Dieterle, et al., 2007; Grochowiecki, et al., 2006; Larsen, et al., 2004; Knoll and Nichol, 2003; Reddy, et al., 2003; Bunnapradist, et al., 2003; Sureshkumar, et al., 2002; Humar, et al., 2001). Morath et al. (2009) reported that evidence suggests longstanding normoglycemia can halt or even reverse diabetic lesions in various organs such as the heart and kidney, surgical complication rates are low, and with potent immunosuppressive medication long term allograft and patient survival are excellent (Morath, et al., 2009). SPK and PAK is a well established and accepted method of treatment for these individuals.

Pancreas Transplantation Alone (PTA)
Pancreas transplantation alone (PTA) may be indicated for individuals who have uncontrolled type 1 DM (i.e., abnormal hemoglobin A_{1c}, inability to maintain blood glucose levels in the normal range) but adequate renal function. The purpose of PTA is to control blood glucose levels and to prevent diabetes-related complications of retinopathy, neuropathy or end-stage renal disease.

Evidence in the published scientific literature is mixed regarding survival rates and improved outcomes associated with PTA (Venstrom, et al., 2003; Gruessner, et al., 2004); however, most patients who undergo PTA achieve insulin independence.

Retransplantation
Due to surgical and immunological problems, graft failure after transplantation is high. Complications related to vascular problems, urologic problems, exocrine pancreatic drainage, pancreatitis and wound infections have been reported in the literature. More recently however, it has been noted that improvements in preservation, technical aspects of the procedure and newer immunosuppressive therapies have led to reduced graft failure rates (Ming and Chen, 2007).

For all three types of pancreas transplants, survival rates for a second transplant are lower than for the primary transplant, although an elective retransplant may be considered suitable for a select group of patients. Various authors have reported outcomes for pancreas retransplant in the literature (Humar, et al., 2000; International Pancreas Transplant Registry, 2004; Genzini, et al.2006; Sansalone et al., 2006; Fellmer, et al., 2007). According to the registry, there was no significant difference in graft survival rates for all types of pancreas retransplant. For SPK however there was a significant difference between retransplant and primary transplant at one year (69% versus 84.7%, respectively). Pancreas graft survival rates for PAK and PTA retransplant were similar to primary transplants (77% versus 78.5%, and 73% versus 78.2%, respectively). The medical literature suggests in some patients, a retransplant could improve health outcomes after graft loss, although there is insufficient data regarding health outcomes associated with third and subsequent pancreas transplants to allow strong conclusions.

Professional Societies/Organizations

American Diabetes Association (ADA): Based on a technical review, the American Diabetes Association (ADA) has adopted the position that PTA should only be considered in type 1 diabetic patients who exhibit the three following criteria: 1) a history of frequent, acute and severe metabolic complications (e.g., hypoglycemia, hyperglycemia and ketoacidosis) requiring medical attention; 2) incapacitating clinical and emotional problems with exogenous insulin therapy; and 3) acute complications despite insulin-based management. Furthermore, pancreas transplantation should be considered an acceptable therapeutic alternative to continued insulin therapy in diabetic patients with imminent or established ESRD who have had or plan to have a kidney transplant, because the successful addition of a pancreas does not jeopardize patient survival, may improve kidney survival, and will restore normal glycemia. Although there is no recent update, the ADA position statement did not address segmental versus whole organ transplant (Robertson, et al., 2006).

An official position statement regarding the use of C-peptide criteria for distinguishing between type I and type II DM could not be found for either the American Association of Clinical Endocrinologists or the ADA. However, according to the National Coverage Determination (NCD) for "Pancreas Transplant", the Centers for Medicare and Medicaid Services (CMS) has defined type I diabetes as "patients that are beta-cell autoantibody positive" or "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". In the context of the NCD, they further clarify that fasting C-peptide levels will only be considered valid with a concurrently obtained fasting glucose $\leq$225 mg/dL."

Contraindications to Kidney Transplantation, Pancreas-Kidney Transplantation, and Pancreas Transplant Alone

Many factors affect the outcome of a solid organ transplant. A fairly rigid selection process is required in order to obtain the best result for each patient. In addition to the absolute contraindications noted in the Coverage Position above, relative contraindications to pancreas or pancreas-kidney transplantation include, but are not limited to, the following (Becker, 2012; Bunnapradist, 2007; Knoll, 2005; Hillerman, 2002; Danovitch, 2001; Kaisiske, 2001;Steinman, 2001):

- active substance abuse within the last six months, including tobacco, alcohol and narcotic/other addictive pain medications
- potential complications from immunosuppressive medications that are unacceptable to the patient
- cerebrovascular disease or accident or progressive neuropathy or myopathy that is not amenable to rehabilitation
- body mass index (BMI) less than 17 or greater than 33
- any active medical process that is currently not optimally treated and/or stable and that is likely to result in end-organ damage or medical emergency without appropriate management, such as active peptic ulcer disease, diverticular disease, active hepatitis, cholecystitis, pancreatitis, hypertension, autoimmune disease or cytopenia
- untreated osteoporosis with a T-score greater than 2.5 standard deviations (SD) from mean or Z-score greater than two SD from mean
- hepatic fibrosis or cirrhosis
- hepatitis C with biopsy-proven, histologic evidence of hepatic disease
- uncorrected abdominal aortic aneurysm greater than four centimeters
- advanced age
- peripheral vascular disease not amenable to surgical or percutaneous therapy as evidenced by:
    - asymptomatic stenosis greater than 75% or symptomatic carotid stenosis of less severity
    - ankle brachial index less than 0.7 or substantial risk of limb loss with diminished perfusion
- systemic infection making immune response risky, including human immunodeficiency virus (HIV), hepatitis B virus (HBV) in the recipient or cytomegalovirus (CMV) in the donor

Additionally, there are other conditions that may affect the outcome of kidney transplantation, pancreas-kidney transplantation and pancreas alone transplantation and require further investigation to ensure the best chance for successful transplantation:

- history of recurrent infection or bladder dysfunction indicates the need for a urological evaluation

- potential for renal malignancy should be screened by use of magnetic resonance imaging (MRI), computed tomography (CT) or renal ultrasound
- reflux nephropathy, history of recurrent infections, nephrolithiasis, heavy proteinuria, hypertension resistant to therapy, or enlarged or symptomatic polycystic kidneys should be evaluated for potential nephrectomy

For pancreas-kidney transplantation further investigation for the following should occur to ensure the best chance for successful pancreas-kidney transplantation:

- autosomal dominant polycystic kidney disease (ADPKD): high-resolution CT or MRI to evaluate for intracranial aneurysms

Bioartificial Pancreas
Bioartificial pancreas devices are currently being investigated by some authors. In theory, the technology involves transplanting healthy islet cells (pancreatic cells that release insulin) into a subject with diabetes; current studies consist mainly of animal trials. Islet cell sources include human or allogeneic cells, porcine or xenographic cells, and engineered cells. The islet cells are encapsulated with a semipermeable membrane, such as hydrogel or polymer, and are then placed in the body. Authors contend the bioartificial pancreas device acts a substitute for the endocrine portion of the pancreas, avoiding obstacles in islet cell transplantation which include limited supply and immunosuppressive drug therapy. The optimal site for implantation has not been clearly defined, although the intended use is for implantation into a vascular site or the peritoneal cavity.

Use Outside of the US: No relevant information.

Summary
Kidney transplantation is an accepted and successful treatment for many individuals with end-stage renal disease (ESRD). The transplant evaluation should begin when it is clear that the patient is destined to develop ESRD. In the event of subsequent renal graft failure, retransplantation is often performed.

Pancreas transplantation has been demonstrated to improve the quality of life of people with diabetes, primarily by eliminating acute complications. Pancreas transplantation alone (PTA) and pancreas transplant after kidney transplant (PAK) are viable options in the management of patients with uncontrolled or severely disabling type I diabetes mellitus (DM) with adequate renal function. Simultaneous pancreas kidney transplant (SPK) is considered a treatment option for individuals with type I DM who have already developed ESRD or for whom ESRD is inevitable. There is insufficient evidence in the peer reviewed scientific literature to support safety and efficacy for living donor pancreas transplantation and bioartificial pancreas devices.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

Kidney Transplantation

Covered when medically necessary:

CPT®* Codes	Description
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
50328	Backbench reconstruction of cadaver or living donor renal allograft prior to transplantation; arterial anastomosis, each
50329	Backbench reconstruction of cadaver or living donor renal allograft prior to transplantation; ureteral 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
50547	Laparoscopy, surgical; donor nephrectomy (including cold preservation), from living donor

HCPCS Codes	**Description**
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 pre- and post-transplant care in the global definition

Simultaneous Pancreas-Kidney Transplantation

Covered when medically necessary:

CPT®* Codes	**Description**
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
50328	Backbench reconstruction of cadaver or living donor renal allograft prior to transplantation; arterial anastomosis, each
50329	Backbench reconstruction of cadaver or living donor renal allograft prior to transplantation; ureteral 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
50547	Laparoscopy, surgical; donor nephrectomy (including cold preservation), from living donor

HCPCS Codes	**Description**
S2065	Simultaneous pancreas kidney transplantation
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 pre- and post-transplant care in the global definition

Pancreas-After-Kidney Transplantation

Covered when medically necessary:

CPT®* Codes	**Description**
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

HCPCS Codes	**Description**
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 pre- and post-transplant care in the global definition

Pancreas Transplantation Alone

Covered when medically necessary:

CPT®* Codes	**Description**
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

HCPCS Codes	Description
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 pre- and post-transplant care in the global definition

Experimental, Investigational/Unproven/Not Covered when used to report living donor pancreas transplantation (i.e., partial pancreas transplantation, segmental pancreas transplantation):

CPT®* Codes	Description
48999	Unlisted procedure, pancreas

Experimental, Investigational/Unproven/Not Covered when used to report bioartificial pancreas device:

HCPCS Codes	Description
L8699	Prosthetic implant, not otherwise specified

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