Allogeneic Pancreas Transplant

Description

Transplantation of a healthy pancreas is a treatment for patients with insulin-dependent diabetes. Pancreas transplantation can restore glucose control and prevent, halt, or reverse the secondary complications from diabetes.

OBJECTIVE

The objective of this evidence review is to determine whether pancreas transplantation or retransplantation improves the net health outcome in patients with insulin-dependent diabetes compared with standard management without transplantation.

POLICY STATEMENT

Pancreas transplant after a prior kidney transplant may be considered medically necessary in patients with insulin-dependent diabetes.

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A combined pancreas and kidney transplant may be considered **medically necessary** in insulin-dependent diabetic patients with uremia.

Pancreas transplant alone may be considered **medically necessary** in patients with severely disabling and potentially life-threatening complications due to hypoglycemia unawareness and labile insulin-dependent diabetes that persists despite optimal medical management.

Pancreas retransplant after a failed primary pancreas transplant may be considered **medically necessary** in patients who meet criteria for pancreas transplantation.

Pancreas transplant is considered **investigational** in all other situations.

**POLICY GUIDELINES**

**General Criteria**

Potential contraindications for solid organ transplant are subject to the judgment of the transplant center include the following:

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

**Pancreas-Specific Criteria**

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

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

Additionally, most pancreas transplant patients will have type 1 diabetes. Those transplant candidates with type 2 diabetes, in addition to being insulin-dependent, should also not be obese (body mass index should be ≤32 kg/m²). According to International Pancreas Transplant Registry data, in 2010, 7% of pancreas transplant recipients had type 2 diabetes (Gruessner [2011]).

**Multiple Transplant Criteria**

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

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

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BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA REGULATORY STATUS

Small bowel/liver and multivisceral transplantation are surgical procedures and, as such, are not subject to regulation by the U.S. Food and Drug Administration.

The U.S. Food and Drug Administration regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation Title 21, parts 1270 and 1271. Pancreas transplants are included in these regulations.

RATIONALE

Summary of Evidence

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

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

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

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

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

Organ Procurement and Transplantation Network

The Organ Procurement and Transplantation Network updated its comprehensive list of transplant-related policies, most recently in May 2019.23.
For pancreas registration:

"Each candidate registered on the pancreas waiting list must meet one of the following requirements:

- Be diagnosed with diabetes
- Have pancreatic exocrine insufficiency
- Require the procurement or transplantation of a pancreas as part of a multiple organ transplant for technical reasons."

For combined kidney plus pancreas registration: "Each candidate registered on the kidney-pancreas waiting list must be diagnosed with diabetes or have pancreatic exocrine insufficiency with renal insufficiency."

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

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

"A. General

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

B. Nationally Covered Indications

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

Effective ... 2006, pancreas transplants alone (PA) are reasonable and necessary for Medicare beneficiaries in the following limited circumstances:

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

Nationally non-covered indications include "Transplantation of partial pancreatic tissue or islet cells (except in the context of a clinical trial)."

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REFERENCES


**POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:**

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<td>Replace</td>
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<td>References 7, and 14 added; other references renumbered or removed.</td>
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<td>Statement added that pancreas transplant is investigational in all other situations.</td>
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<tr>
<td>June 2015</td>
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