Protocol

Allogeneic Pancreas Transplant

(70302)

Medical Benefit		**Effective Date**: 07/01/14	**Next Review Date**: 05/19
Preauthorization	Yes	**Review Dates**: 09/09, 09/10, 09/11, 07/12, 05/13, 05/14, 05/15, 05/16, 05/17, 05/18	

Preauthorization is required and must be obtained through Case Management.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: • With insulin-dependent diabetes	Interventions of interest are: • Pancreas transplant after a kidney transplant	Comparators of interest are: • Insulin therapy	Relevant outcomes include: • Overall survival • Change in disease status • Treatment-related mortality • Treatment-related morbidity
Individuals: • With insulin-dependent diabetes with uremia	Interventions of interest are: • Simultaneous pancreas and kidney transplant	Comparators of interest are: • Insulin therapy	Relevant outcomes include: • Overall survival • Change in disease status • Treatment-related mortality • Treatment-related morbidity
Individuals: • With insulin-dependent diabetes and severe complications	Interventions of interest are: • Pancreas transplant alone	Comparators of interest are: • Insulin therapy	Relevant outcomes include: • Overall survival • Change in disease status • Treatment-related mortality • Treatment-related morbidity
Individuals: • With a prior pancreas transplant who meet still criteria for a pancreas transplant	Interventions of interest are: • Pancreas retransplant	Comparators of interest are: • Insulin therapy	Relevant outcomes include: • Overall survival • Change in disease status • Treatment-related mortality • Treatment-related morbidity

DESCRIPTION

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

SUMMARY OF EVIDENCE

For individuals who have insulin-dependent diabetes who receive a pancreas transplant after a kidney transplant, the evidence includes case series and registry studies. Relevant outcomes are overall survival, 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 transplant after a kidney transplant (e.g., a three-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 pancreas transplant after a kidney transplant or a simultaneous pancreas and 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 transplant, the evidence includes registry studies. Relevant outcomes are overall survival, 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, the evidence includes registry studies. Relevant outcomes are overall survival, 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 pancreas transplant alone have improved over time (e.g., three-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. Relevant outcomes are overall survival, change in disease status, and treatment-related mortality and morbidity. National data and data reported from specific transplant centers 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.

POLICY

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

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 in spite of 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

Individual transplant facilities may have their own *additional* requirements or protocols that must be met in order for the patient to be eligible for a transplant at their facility.

Potential contraindications subject to the judgment of the transplant center:

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

PANCREAS SPECIFIC CRITERIA

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

- Documentation of severe hypoglycemia unawareness as evidenced by chart notes or emergency department visits; OR
- Documentation of 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 mellitus. Those transplant candidates with type 2 diabetes mellitus, in addition to being insulin-dependent, should also not be obese (body mass index [BMI] should be 32 or less). According to International Registry data, in 2010, 7% of pancreas transplant recipients had type 2 diabetes (Gruessner, 2012).

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.

MEDICARE ADVANTAGE

If a transplant is needed, we arrange to have the Medicare–approved transplant center review and decide whether the patient is an appropriate candidate for the transplant.

BACKGROUND

DIABETES AND PANCREATITIS

Achievement of insulin independence with resultant decreased morbidity and increased quality of life is the primary health outcome of pancreas transplantation. While pancreas transplantation is generally not considered a life-saving treatment, in a small subset of patients who experience life-threatening complications from diabetes, pancreas transplantation could be considered life-saving. Pancreas transplant alone (PTA) has also been investigated in patients following total pancreatectomy for chronic pancreatitis. In addition to the immune

rejection issues common to all allograft transplants, autoimmune destruction of beta cells has been observed in the transplanted pancreas, presumably from the same mechanism responsible for type 1 diabetes.[1]

Treatment

Pancreas transplantation occurs in several different scenarios such as (1) a diabetic patient with renal failure who may receive a simultaneous cadaveric pancreas plus kidney transplants; (2) a diabetic patient who may receive a cadaveric or living-related pancreas transplant after a kidney transplantation (pancreas after kidney); or (3) a nonuremic diabetic patient with specific severely disabling and potentially life-threatening diabetic problems who may receive a PTA. The total number of adult pancreas transplants (pancreas and pancreas plus kidney) in the United States peaked at 1484 in 2004; the number has since declined.[2] In 2016, 215 PTAs and 798 SPK were performed in the United States.[2]

Most patients undergoing PTA are those with either hypoglycemic unawareness or labile diabetes. However, other exceptional circumstances may exist where nonuremic type 1 diabetes patients have significant morbidity risks due to secondary complications of diabetes (e.g., peripheral neuropathy) that exceed those of the transplant surgery and subsequent chronic immunosuppression. Because virtually no published evidence addressing outcomes of medical management in this very small group of exceptional diabetic patients, it is not possible to generalize about which circumstances represent appropriate indications for pancreas transplantation alone. Case-by-case consideration of each patient's clinical situation may be the best option for determining the balance of risks and benefits.

According to International Pancreas Transplant Registry data, the proportion of pancreas transplant recipients worldwide who have type 2 diabetes has increased over time, from 2% in 1995 to 7% in 2010.[3] In 2010, approximately 8% of SPK transplants, 5% of pancreas transplant after kidney transplant, and 1% of PTA were performed in patients with type 2 diabetes.

The approach to retransplantation varies by cause of failure. Surgical and technical complications such as venous thrombosis are the leading cause of pancreatic graft loss among diabetic patients. Graft loss from chronic rejection may result in sensitization, increasing both the difficulty of finding a cross-matched donor and the risk of rejection of a subsequent transplant. Each transplant center has guidelines based on experience; some centers may wait to allow reconstitution of the immune system before initiating retransplant with an augmented immunosuppression protocol.

REGULATORY STATUS

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.

RELATED PROTOCOLS

Artificial Pancreas Device Systems

Islet transplantation

Kidney Transplant

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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