Allogeneic Pancreas Transplant

Policy # 00092
Original Effective Date: 11/22/1993
Current Effective Date: 02/13/2023

 Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Islet cell transplantation is considered in medical policy 00007.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

• Benefits are available in the member’s contract/certificate, and
• Medical necessity criteria and guidelines are met.

Based on review of available data, the Company may consider a combined pancreas-kidney transplant in insulin dependent diabetic individuals with uremia to be eligible for coverage.**

Based on review of available data, the Company may consider pancreas transplant after a prior kidney transplant in individuals with insulin dependent diabetes to be eligible for coverage.**

Based on review of available data, the Company may consider pancreas transplant alone in individuals 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 to be eligible for coverage.**

Based on review of available data, the Company may consider pancreas retransplant after a failed primary pancreas transplant in individuals who meet criteria for pancreas transplantation to be eligible for coverage.**

Pancreas transplantation, when the transplant recipient is human immunodeficiency virus (HIV) positive, may be considered for coverage when all of the additional criteria are met:

• CD4 count >200 cells/mm-3 for more than six months; and
• Undetectable HIV viremia (<50 HIV-1 RNA copies/mL) for at least six months; and
• Demonstrable adherence and a stable HAART regimen for at least six months; and

©2023 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.
Allogeneic Pancreas Transplant

Policy # 00092
Original Effective Date: 11/22/1993
Current Effective Date: 02/13/2023

- Absence of AIDS-defining illness following successful immune reconstitution after HAART; and
- All other transplant criteria are met.

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

The use of pancreas transplant when patient selection criteria are not met is considered investigational.*

The use of pancreas transplant in HIV positive recipients when patient selection criteria and additional HIV positive patient selection criteria are not met is considered investigational.*

Based on review of available data, pancreas re-transplantation after two or more prior failed pancreas transplants is considered investigational.*

Policy Guidelines

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

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 diseases 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 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:
Allogeneic Pancreas Transplant

Policy #    00092
Original Effective Date: 11/22/1993
Current Effective Date: 02/13/2023

- 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. 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). In 2018, patients with type 2 diabetes accounted for 14.8% of all pancreas transplants, according to data from the Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients.

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 (eg, 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.

Background/Overview
Solid Organ Transplantation
Solid organ transplantation offers a treatment option for patients with different types of end-stage organ failure that can be lifesaving or provide significant improvements to a patient’s quality of life. Many advances have been made in the last several decades to reduce perioperative complications. Available data supports improvement in long-term survival as well as improved quality of life particularly for liver, kidney, pancreas, heart, and lung transplants. Allograft rejection remains a key early and late complication risk for any organ transplantation. Transplant recipients require life-long immunosuppression to prevent rejection. Patients are prioritized for transplant by mortality risk and severity of illness criteria developed by the Organ Procurement and Transplantation Network and United Network of Organ Sharing.
Allogeneic Pancreas Transplant

Policy # 00092
Original Effective Date: 11/22/1993
Current Effective Date: 02/13/2023

Allogeneic Pancreas Transplant
In 2021, 41,355 transplants were performed in the United States procured from more than 13,800 deceased donors and 6,500 living donors. Pancreas-kidney transplants were the fifth most common procedure, with 820 transplants performed in 2021. Pancreas-alone transplants were the sixth most common procedure, with 143 transplants performed in 2021.

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 transplant; (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 pancreas transplant alone.

Data from the United Network for Organ Sharing and the International Pancreas Transplant Registry indicate that the proportion of simultaneous pancreas plus kidney transplant recipients worldwide who have type 2 diabetes has increased over time, from 6% of transplants between 2005 and 2009 to 9% of transplants between 2010 and 2014. Between 2010 and 2014, approximately 4% of pancreas after kidney transplants and 4% of pancreas alone transplants were performed in patients with type 2 diabetes. In 2019, patients with type 2 diabetes accounted for 20.6% of all pancreas transplants, according to data from the Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients. Patients with type 2 diabetes accounted for 6.2%, 1%, and 22.4% of pancreas alone, pancreas after kidney, and simultaneous pancreas plus kidney transplants, respectively.

FDA or Other Governmental Regulatory Approval
U.S. Food and Drug Administration (FDA)
Solid organ transplants are a surgical procedure and, as such, are not subject to regulation by the U.S. FDA.

The FDA 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. Solid organs used for transplantation are subject to these regulations.
Allogeneic Pancreas Transplant

Policy # 00092
Original Effective Date: 11/22/1993
Current Effective Date: 02/13/2023

**Rationale/Source**
This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

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.

**Summary of Evidence**
For individuals who have insulin-dependent diabetes who receive a pancreas transplant after a kidney transplant, the evidence includes retrospective studies and registry studies. 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 transplant after a kidney transplant (e.g., a 3-year survival rate of 94.5%). Single-center retrospective studies have 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 an improvement in the net health outcome.

For individuals who have insulin-dependent diabetes with uremia who receive SPK transplants, the evidence includes retrospective studies and registry studies. 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 versus those on a waiting list. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have insulin-dependent diabetes and severe complications who receive a pancreas transplant alone, the evidence includes registry studies. Relevant outcomes are OS, change in disease status, and treatment-related mortality and morbidity. Data from international and national...
Allogeneic Pancreas Transplant

Policy # 00092
Original Effective Date: 11/22/1993
Current Effective Date: 02/13/2023

registries have found that graft and patient survival rates after pancreas transplant alone have improved over time (e.g., 3-year survival of 94.9%). The evidence is sufficient to determine that the technology results in an 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 retrospective studies and registry studies. 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 an improvement in the net health outcome.

**Supplemental Information**

**Practice Guidelines and Position Statements**

Guidelines or position statements will be considered for inclusion in ‘Supplemental Information’ if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

**Organ Procurement and Transplantation Network**

The Organ Procurement and Transplantation Network updated its comprehensive list of transplant-related policies, most recently in April 2022.

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."
Allogeneic Pancreas Transplant

Policy # 00092
Original Effective Date: 11/22/1993
Current Effective Date: 02/13/2023

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.
2. Patients must have a diagnosis of type I diabetes:
   • Patient with diabetes must be beta-cell autoantibody-positive; or
   • 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 noncovered indications include "Transplantation of partial pancreatic tissue or islet cells (except in the context of a clinical trial)."

Ongoing and Unpublished Clinical Trials
Some currently ongoing and unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ongoing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01047865</td>
<td>Recurrence of T1D in Pancreas Transplantation</td>
<td>400</td>
<td>May 2023</td>
</tr>
<tr>
<td>NCT01957696</td>
<td>A Prospective, Observational Study in Pancreatic Allograft Recipients: The Effect of Risk Factors, Immunosuppressive Level and the Benefits of Scheduled Biopsies - on Surgical Complications, Rejections and Graft Survival</td>
<td>80</td>
<td>Oct 2028</td>
</tr>
</tbody>
</table>
Allogeneic Pancreas Transplant

Policy # 00092
Original Effective Date: 11/22/1993
Current Effective Date: 02/13/2023

<table>
<thead>
<tr>
<th>NCT03921593</th>
<th>Prospective Longitudinal Observational Study on Insulin Dependent Diabetic Patients Undergoing Any Form of Solid Organ Pancreas Transplantation Aimed to Clarify Quality of Life Changes After Pancreas Transplantation</th>
<th>110</th>
<th>Mar 2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unpublished</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT00238693</td>
<td>Transplant Registry: Patients Who May Require Transplantation and Those Who Have Undergone Transplantation of Liver, Kidney and/or Pancreas</td>
<td>13,767</td>
<td>Aug 2018</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

References

Allogeneic Pancreas Transplant

Policy #  00092
Original Effective Date:  11/22/1993
Current Effective Date:  02/13/2023


©2023 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.
Allogeneic Pancreas Transplant

Policy # 00092
Original Effective Date: 11/22/1993
Current Effective Date: 02/13/2023

30. Gruessner AC, Sutherland DE. Access to pancreas transplantation should not be restricted because of age: invited commentary on Schenker et al. Transpl Int. Feb 2011; 24(2): 134-5. PMID 21208293

Policy History
Original Effective Date: 11/22/1993
Allogeneic Pancreas Transplant

Policy # 00092
Original Effective Date: 11/22/1993
Current Effective Date: 02/13/2023

Current Effective Date: 02/13/2023
11/21/2001 Managed Care Advisory Council approval
11/18/2003 Medical Policy Committee review
01/26/2004 Managed Care Advisory Council approval
01/04/2005 Medical Director review
01/18/2005 Medical Policy Committee review. Format revision. No substance change to policy.
01/31/2005 Managed Care Advisory Council approval
02/01/2006 Medical Director review
03/15/2006 Medical Policy Committee approval. Format revision.
02/07/2007 Medical Director review
02/21/2007 Medical Policy Committee approval. Coverage eligibility unchanged.
02/13/2008 Medical Director review
02/20/2008 Medical Policy Committee approval.
02/04/2009 Medical Director review
02/19/2009 Medical Policy Committee approval. Clarified 2nd, 3rd and 4th criteria bullets for HIV positive transplant recipients. No change to coverage eligibility.
02/04/2010 Medical Policy Committee approval
02/17/2010 Medical Policy Implementation Committee approval. No change to coverage.
02/03/2011 Medical Policy Committee approval
02/16/2011 Medical Policy Implementation Committee approval. No change to coverage.
02/02/2012 Medical Policy Committee approval
02/15/2012 Medical Policy Implementation Committee approval. Patient selection criteria revised.
01/03/2013 Medical Policy Committee approval
01/09/2013 Medical Policy Implementation Committee approval. No change to coverage.
01/09/2014 Medical Policy Committee approval
01/15/2014 Medical Policy Implementation Committee approval. Patient selection criteria section removed.
01/08/2015 Medical Policy Committee approval
01/21/2015 Medical Policy Implementation Committee approval. Added “in patients who meet criteria for pancreas transplantation” in the criteria for pancreas retransplant after a failed primary pancreas transplant.
01/07/2016 Medical Policy Committee approval
01/22/2016 Medical Policy Implementation Committee approval. No change to coverage.
Allogeneic Pancreas Transplant

Policy # 00092
Original Effective Date: 11/22/1993
Current Effective Date: 02/13/2023

01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes
01/05/2017 Medical Policy Committee approval
01/18/2017 Medical Policy Implementation Committee approval. No change to coverage
01/04/2018 Medical Policy Committee approval
01/17/2018 Medical Policy Implementation Committee approval. No change to coverage. Added policy guidelines.
01/10/2019 Medical Policy Committee approval
01/23/2019 Medical Policy Implementation Committee approval. No change to coverage
01/03/2020 Medical Policy Committee review
01/08/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/07/2021 Medical Policy Committee review
01/13/2021 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/06/2022 Medical Policy Committee review
01/12/2022 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/05/2023 Medical Policy Committee review
01/11/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 01/2024

Coding
The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®), copyright 2022 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines.
Allogeneic Pancreas Transplant

Policy # 00092
Original Effective Date: 11/22/1993
Current Effective Date: 02/13/2023

Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

<table>
<thead>
<tr>
<th>Code Type</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>48550, 48551, 48552, 48554, 48556</td>
</tr>
<tr>
<td>HCPCS</td>
<td>S2065, S2152</td>
</tr>
<tr>
<td>ICD-10 Diagnosis</td>
<td>All related diagnoses</td>
</tr>
</tbody>
</table>

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with technology evaluation center(s);
Allogeneic Pancreas Transplant

Policy # 00092
Original Effective Date: 11/22/1993
Current Effective Date: 02/13/2023

2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or

3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

©2023 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.