MEDICAL POLICY – 7.03.12
Islet Transplantation

BCBSA Ref. Policy: 7.03.12
Effective Date: Oct. 1, 2018
Last Revised: Oct. 10, 2018
Replaces: N/A

RELATED MEDICAL POLICIES:
None

Introduction

The pancreas is an organ that stretches lengthwise across the abdominal area below the stomach. Within the pancreas are cell clusters commonly called “the islets.” Included in the islets are beta cells which make, store, and release insulin. Treating chronic inflammation of the pancreas may mean removing the pancreas. Removing the pancreas also removes the islets and the beta cells, which then leads to type 1 diabetes. To prevent the development of type 1 diabetes in people who have their pancreas removed, their own islet cells can be harvested and injected into a specific vein in the liver. Published medical studies show that islet cell transplantation appears to significantly decrease the development of diabetes after the pancreas is removed. In this situation, islet cell transplantation may be considered medically necessary. Islet cell transplantation using donor cells is being studied as a technique to treat existing type 1 diabetes. There is not enough medical evidence to show how well this works to treat type 1 diabetes. Larger and longer studies are needed. For these reasons, islet cell transplantation to treat existing type 1 diabetes is investigational (unproven).

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.
Policy Coverage Criteria

### Procedure | Medical Necessity
--- | ---
Autologous pancreas islet transplantation | Autologous pancreas islet transplantation may be considered medically necessary as an adjunct to a total or near total pancreatectomy in patients with chronic pancreatitis.

### Procedure | Investigational
--- | ---
Allogeneic islet transplantation | Allogeneic islet transplantation is considered investigational for the treatment of type 1 diabetes.
Islet transplantation, all other | Islet transplantation is considered investigational in all other situations.

### Documentation Requirements
The patient’s medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following:
- Office visit notes that contain the relevant history and physical:
  - Patient had pancreas removed because of chronic pancreatitis

### Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>Pancreatectomy, total or subtotal, with autologous transplantation of pancreas or pancreatic islet cells</td>
</tr>
<tr>
<td>48160</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>HCPCS</th>
<th>Description</th>
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<tbody>
<tr>
<td>G0341</td>
<td>Percutaneous islet cell transplant, includes portal vein catheterization and infusion</td>
</tr>
<tr>
<td>G0342</td>
<td>Laparoscopy for islet cell transplant, includes portal vein catheterization and infusion</td>
</tr>
<tr>
<td>G0343</td>
<td>Laparotomy for islet cell transplant, includes portal vein catheterization and infusion</td>
</tr>
<tr>
<td>S2102</td>
<td>Islet cell tissue transplant from pancreas; allogeneic</td>
</tr>
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</table>
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Related Information

N/A

Evidence Review

Description

Performed in conjunction with pancreatectomy, autologous islet transplantation is proposed to reduce the likelihood of insulin-dependent diabetes. Allogeneic islet cell transplantation is being investigated as a treatment or cure for patients with type 1 diabetes.

Background

Chronic Pancreatitis

Primary risk factors for chronic pancreatitis may be categorized as the following: toxic-metabolic, idiopathic, genetic, autoimmune, recurrent and severe acute pancreatitis, or obstructive (TIGAR-O classification system). Patients with chronic pancreatitis may experience intractable pain that can only be relieved with a total or near total pancreatectomy. However, the pain relief must be balanced against the certainty that the patient will be rendered an insulin-dependent diabetic.

Type 1 Diabetes

Glucose control is a challenge for individuals with type 1 diabetes. Failure to prevent disease progression can lead to long-term complications such as retinopathy, neuropathy, nephropathy, and cardiovascular disease.¹
**Islet Transplantation**

In autologous islet transplantation during the pancreatectomy procedure, islet cells are isolated from the resected pancreas using enzymes, and a suspension of the cells is injected into the portal vein of the patient’s liver. Once implanted, the beta cells in these islets begin to make and release insulin.

Allogeneic islet transplantation potentially offers an alternative to whole-organ pancreas transplantation. In the case of allogeneic islet cell transplantation, cells are harvested from a deceased donor’s pancreas, processed, and injected into the recipient’s portal vein. Up to 3 donor pancreas transplants may be required to achieve insulin independence. However, a limitation of islet transplantation is that 2 or more donor organs are usually required for successful transplantation, although experimentation with single-donor transplantation is occurring. A pancreas that is rejected for whole-organ transplant is typically used for islet transplantation. Therefore, islet transplantation has generally been reserved for patients with frequent and severe metabolic complications who have consistently failed to achieve control with insulin-based management. Allogeneic transplantation may be performed in the radiology department.

In 2000, a modified immunosuppression regimen increased the success of allogeneic islet transplantation. This regimen is known as the “Edmonton protocol.”

**Summary of Evidence**

For individuals with chronic pancreatitis undergoing total or near total pancreatectomy who receive autologous pancreas islet transplantation, the evidence includes case series and systematic reviews. Relevant outcomes are overall survival, change in disease status, medication use, resource utilization, and treatment-related morbidity. Autologous islet transplants are performed in the context of total or near total pancreatectomies to treat intractable pain for chronic pancreatitis. The procedure appears to significantly decrease the incidence of diabetes after total or near total pancreatectomy in patients with chronic pancreatitis. Also, this islet procedure is not associated with serious complications and is performed in patients who are already undergoing a pancreatectomy procedure. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with type 1 diabetes who receive allogeneic pancreas islet transplantation, the evidence includes an RCT, case series, and systematic reviews. Relevant outcomes are overall
survival, change in disease status, medication use, resource utilization, and treatment-related morbidity. Results of a 2018 randomized trial have suggested some reduction in the number of severe hypoglycemic incidence annually, but limited follow-up and other trial limitations reduce the certainty in conclusions drawn. A wide range of insulin independence has been reported in case series. There is conflicting evidence whether allogeneic islet transplantation reduces long-term diabetic complications. Long-term comparative studies are required to determine the effects of allogeneic islet transplantation in type 1 diabetics. The evidence is insufficient to determine the effects of the technology on health outcomes.

Ongoing and Unpublished Clinical Trials

Some currently 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>
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<tbody>
<tr>
<td>Ongoing</td>
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<tr>
<td>NCT02505893</td>
<td>Minimal Islet Transplant at Diabetes Onset (MITO)</td>
<td>6</td>
<td>May 2018 (ongoing)</td>
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<tr>
<td>NCT00160732</td>
<td>Allogenic Islet Cell Transplantation</td>
<td>50</td>
<td>Oct 2018</td>
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<tr>
<td>NCT00706420</td>
<td>Islet Transplantation Alone (ITA) in Patients With Difficult to Control Type I Diabetes Mellitus Using a Glucocorticoid-free Immunosuppressive Regimen</td>
<td>20</td>
<td>Apr 2019</td>
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<tr>
<td>NCT00306098</td>
<td>Islet Cell Transplantation Alone in Patients With Type 1 Diabetes Mellitus: Steroid-Free Immunosuppression</td>
<td>40</td>
<td>May 2020</td>
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<tr>
<td>NCT01909245</td>
<td>Islet Cell Transplant for Type 1 Diabetes (TCD)</td>
<td>30</td>
<td>Jul 2021</td>
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<tr>
<td>NCT01974674</td>
<td>Allogeneic Islet Transplantation for the Treatment of Type 1 Diabetes (GRIIF)</td>
<td>19</td>
<td>Jan 2022</td>
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<tr>
<td>NCT01897688</td>
<td>A Phase 3 Single Center Study of Islet Transplantation in Non-uremic Diabetic Patients</td>
<td>40</td>
<td>Mar 2027</td>
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<tr>
<td>NCT00679042</td>
<td>Islet Transplantation in Type 1 Diabetic Patients Using the University of Illinois at Chicago (UIC) Protocol</td>
<td>36</td>
<td>May 2027</td>
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</table>

NCT: national clinical trial.
Practice Guidelines and Position Statements

Guidance from the National Institute for Care Excellence (2008) indicated the evidence on allogeneic pancreatic islet cell transplantation for type 1 diabetes has shown that serious procedure-related complications may occur, and the long-term immunosuppression required is associated with the risk of adverse events.\(^1\) A related 2008 guidance addressed autologous islet cell transplantation for improved glycemic control after pancreatectomy and stated that studies have shown "some short-term efficacy, although most patients require insulin therapy in the long term.... complications result mainly from the major surgery involved in pancreatectomy (rather than from the islet cell transplantation)."\(^2\)

Medicare National Coverage

Medicare covers pancreatic islet transplantation in patients with type 1 diabetes participating in a clinical trial sponsored by the National Institutes of Health.\(^3\) Partial pancreatic tissue transplantation or islet transplantation performed outside a clinical trial are not.

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. Allogeneic islet cells are included in these regulations.

References


<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>03/08/05</td>
<td>Replace Policy - Policy reviewed; added information on islet transplantation for type I diabetes and statement that this indication is considered investigational; added Medicare coverage policy information on islet transplantation for type 1 diabetes; removed “autologous” from the policy title; HCPCS codes updated.</td>
</tr>
<tr>
<td>12/13/05</td>
<td>Replace Policy - Policy reviewed with literature search; reference added. Policy statement and title updated with removal of &quot;cell&quot; when describing islet transplantation rather than &quot;islet cell transplantation.&quot;</td>
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<td>05/26/06</td>
<td>Scope and Disclaimer Updates - No other changes.</td>
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<td>09/12/06</td>
<td>Replace Policy - Policy updated with literature search; no change to policy statement; reference added.</td>
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<tr>
<td>03/11/08</td>
<td>Replace Policy - Policy updated with literature search; no change to policy statement; reference added.</td>
</tr>
<tr>
<td>07/14/09</td>
<td>Replace Policy - Policy updated with literature search; no change to policy statement. Benefit Application section updated. References added.</td>
</tr>
<tr>
<td>09/14/10</td>
<td>Replace Policy - Policy updated with literature review; rationale section extensively edited. References numbers 16 – 18 have been added; the policy statements remain unchanged.</td>
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<tr>
<td>08/09/11</td>
<td>Replace Policy – Policy updated with literature review. Reference numbers 13 and 17 added; other references renumbered or removed; policy statements unchanged. ICD-10 codes added to policy.</td>
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<td>08/20/12</td>
<td>Replace Policy. Rationale section revised based on literature review through April 2012. References 1-3 and 14 added, other references renumbered or removed. Policy statements unchanged.</td>
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<td>09/28/12</td>
<td>Update Coding Section – ICD-10 codes are now effective 10/01/2014.</td>
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<td>01/10/13</td>
<td>Coding update. CPT codes 0141T – 0143T removed from policy; they were deleted as of 1/1/12.</td>
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<tr>
<td>08/16/13</td>
<td>Replace policy. Policy guidelines reformatted for readability. Rationale updated with literature review through April 18, 2013. Ongoing clinical trial added. Reference numbers 7, 9, 11 and 16 added; others renumbered or removed. Policy statements unchanged.</td>
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<tr>
<td>03/11/14</td>
<td>Coding Update. Codes 52.85 and 52.86 were removed per ICD-10 mapping project; these codes are not utilized for adjudication of policy.</td>
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<tr>
<td>07/31/14</td>
<td>Annual Review. Policy updated with literature review through March 26, 2014. Reference numbers 4, 10, 11 and 20 added. Statement added that islet transplantation is considered investigational in all other situations.</td>
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<tr>
<td>07/14/15</td>
<td>Annual Review. Policy updated with literature review through April 8, 2015; references 1, 3, 6, and 11 added. Policy statements unchanged. ICD-9 and ICD-10 procedure codes removed; these were listed for informational purposes only.</td>
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</table>
### Date | Comments
--- | ---
10/01/18 | Annual Review, approved September 20, 2018. Policy updated with literature review through June 2018; references 1 and 10 added. Policy statements unchanged.
10/10/18 | Minor update, added Documentation Requirements section.

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Email AppealsDepartmentInquiries@Premera.com

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Français (French):

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Avi sila a gen Enfòmasyon Empòtan ladan. Avi sila a kapab genyen enfòmasyon enpòtan konpensan aplikasyon w lan oswa konpensan kouvèti ariann lan atravè Premera Blue Cross. Kapab genyen dat ki enpòtan nan avi sila a. Ou ka gen pou pran kék aksyon avan seten dat limit pou ka kenbe kouvèti ariann sante w la oswa pou yo ka ede w ak veék depans yo. Se dwa w pou resewwa enfòmasyon sa a ak asistans nan lang ou pale a, san ou pa gen pou peye pou sa. Rate nan 800-722-1471 (TTY: 800-842-5357).

Deutsche (German):

Hmoob (Hmong):
Tsab ntawv tshaj xo no muaj cov ntshiab lus tseem ceeb. Tjek jaun tsab ntawv tshaj xo no muaj cov ntshiab lus tseem ceeb xog koj daim ntawv thov kev pab los yoj koj qhov kev pab cuam los ntawm Premera Blue Cross. Tjek jaun muaj cov hvnb tseem ceeb uas rau hauv daim ntawm no. Tjek jaun koj yuav tau uu qe yam uas peb koj uas tis pub dhaav cov caij nyong uas teev tseg rau hauv daim ntawv no mas koj thaj yuav tau baais kev pab cuam kho mob los yoj kev pab them tjek niq kho mob ntaw. Koj muaj cai kom lawv muab cov ntshiab lus no uas tau muab sau uas yam lus pub dawb rau koj. Hu rau 800-722-1471 (TTY: 800-842-5357).

Ilokano (Illocano):
Daytoy a Pakdaar ket naglaon iti Napateg nga Impormasion. Daytoy a pakdaar mabalina nga adda ket naglaon iti napateg nga impormasion maipanggepp iti aplikasyono weno coverage babaen iti Premera Blue Cross. Daytoy ket mabalina dagiti importante a pelsa iti daytoy a pakdaar. Mabalina nga adda rumbang nga aramidendo nga adda sakkay dagiti partikular a naituding nga aldaw tapno mapagalatayedge ti coverage ti salan-atyo weno tulong kadagiti gastos. Adda karbangenyo a mangan a daytoy nga impormasion ken tulong iti bukodyo a pagasasao nga awan ti bayadanyo. Tumawag iti numero nga 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):
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