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

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | DOCUMENTATION REQUIREMENTS | CODING
RELATED INFORMATION | EVIDENCE REVIEW | REFERENCES | HISTORY

∞ Clicking this icon returns you to the hyperlinks menu above.

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 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

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Medical Necessity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autologous pancreas islet transplantation</td>
<td>Autologous pancreas islet transplantation may be considered medically necessary as an adjunct to a total or near total pancreatectomy in patients with chronic pancreatitis.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Investigational</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allogeneic islet transplantation</td>
<td>Allogeneic islet transplantation is considered investigational for the treatment of type 1 diabetes.</td>
</tr>
<tr>
<td>Islet transplantation, all other</td>
<td>Islet transplantation is considered investigational in all other situations.</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCPCS</td>
<td></td>
</tr>
<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>
</tbody>
</table>
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>
</tr>
</thead>
<tbody>
<tr>
<td>NCT02505893</td>
<td>Minimal Islet Transplant at Diabetes Onset (MITO)</td>
<td>6</td>
<td>May 2018 (ongoing)</td>
</tr>
<tr>
<td>NCT00160732</td>
<td>Allogenic Islet Cell Transplantation</td>
<td>50</td>
<td>Oct 2018</td>
</tr>
<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>
</tr>
<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>
</tr>
<tr>
<td>NCT01909245</td>
<td>Islet Cell Transplant for Type 1 Diabetes (TCD)</td>
<td>30</td>
<td>Jul 2021</td>
</tr>
<tr>
<td>NCT01974674</td>
<td>Allogeneic Islet Transplantation for the Treatment of Type 1 Diabetes (GRIIF)</td>
<td>19</td>
<td>Jan 2022</td>
</tr>
<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>
</tr>
<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>
</tr>
</tbody>
</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. 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).”

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. 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>
</tr>
</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 &quot;autologous&quot; 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>
</tr>
<tr>
<td>05/26/06</td>
<td>Scope and Disclaimer Updates - No other changes.</td>
</tr>
<tr>
<td>09/12/06</td>
<td>Replace Policy - Policy updated with literature search; no change to policy statement; reference added.</td>
</tr>
<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>
</tr>
<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>
</tr>
<tr>
<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>
</tr>
<tr>
<td>09/28/12</td>
<td>Update Coding Section – ICD-10 codes are now effective 10/01/2014.</td>
</tr>
<tr>
<td>01/10/13</td>
<td>Coding update. CPT codes 0141T – 0143T removed from policy; they were deleted as of 1/1/12.</td>
</tr>
<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>
</tr>
<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>
</tr>
<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>
</tr>
<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>
</tr>
<tr>
<td>Date</td>
<td>Comments</td>
</tr>
<tr>
<td>----------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>10/01/18</td>
<td>Annual Review, approved September 20, 2018. Policy updated with literature review through June 2018; references 1 and 10 added. Policy statements unchanged.</td>
</tr>
<tr>
<td>10/10/18</td>
<td>Minor update, added Documentation Requirements section.</td>
</tr>
</tbody>
</table>

**Disclaimer:** This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2018 Premera All Rights Reserved.

**Scope:** Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.
Discrimination is Against the Law

Premera Blue Cross complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Premera does not exclude people or treat them differently because of race, color, national origin, age, disability or sex.

Premera:
- Provides free aids and services to people with disabilities to communicate effectively with us, such as:
  - Qualified sign language interpreters
  - Written information in other formats (large print, audio, accessible electronic formats, other formats)
- Provides free language services to people whose primary language is not English, such as:
  - Qualified interpreters
  - Information written in other languages

If you need these services, contact the Civil Rights Coordinator.

If you believe that Premera has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance:
- Civil Rights Coordinator - Complaints and Appeals
  PO Box 91102, Seattle, WA 98111
  Toll free 855-332-4535, Fax 425-918-5952. TTY 800-842-5357
  Email AppealsDepartmentinquines@Premera.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:
- U.S. Department of Health and Human Services
  200 Independence Avenue SW, Room 509F, HHH Building
  Washington, DC 20201, 1-800-368-1019, 800-537-7697 (TDD)

Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through Premera Blue Cross. There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost. Call 800-722-1471 (TTY: 800-842-5357).

العربية (Arabic):
يحتوي هذا الإشعار معلومات هامة. قد يحتوي هذا الإشعار معلومات مهمة لمصلحة طبي أو parent.

Premera Blue Cross. قد تكون هناك تراجع مهمة

إذا لم تكن. إنهاء الاختيار في نتائج ممتلكة للمواطنين

نعتنا تأثيرات الغضب. يتضمن ذلك على الخدمات الصحية أو المساواة

لا تتبعها. حدد Executor على هذه المعلومات والملاحظات للمعلومات المقدمة. 

800-722-1471 (TTY: 800-842-5357).

中文 (Chinese):
本通知有重要的訊息。本通知可能會有關於您透過 Premera Blue Cross 提交的申請或保險的重要訊息。本通知可能會有重要日期。您可能需要在截止日期之前採取行動，以保留您的健康保險或費用補貼。您有權利免費以您的母語得到本訊息和幫助。請撥電話 800-722-1471 (TTY: 800-842-5357).

Oromo (Cushite):

Lakooffa bilbilaa 800-722-1471 (TTY: 800-842-5357) tii bilbilaa.

Français (French):

Appelez le 800-722-1471 (TTY: 800-842-5357).

Kreyòl ayisyen (Creole):

Deutsche (German):

Hmoob (Hmong):

Illoko (Ilocano):
Daytoy a Pakdaara ket naglaon iti Napateg nga Impormasion. Daytoy a pakdaara mabalina nga adda ket naglaon iti napateg nga impormasion maiapanggep iti aplikasyonw no coverage babaen iti Premera Blue Cross. Daytoy ket mabalina dagiti importante a pelsa iti daytoy a pakdaara. Mabalina nga adda rumbeng nga aramidenyo nga addang sakkay dagiti particular a naituding nga aldaw tapno mapagtalainayo ti coverage ti salun-aty woy tulong kadagit gastos. Adda karbaganyo a mangala ti daytoy nga impormasion ken tulong iti bukodyo a pagasao nga awan ti bayadanyo. Tumawag ti numero nga hoo 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):
Questo avviso contiene informazioni importanti. Questo avviso può contenere informazioni importanti sulla tua domanda o copertura attraverso Premera Blue Cross. Potrebbero esserci date chiave in questo avviso. Potrebbe essere necessario un tuo intervento entro una scadenza determinata per consentirti di mantenere la tua copertura o sovvenzione. Hai il diritto di ottenere queste informazioni e assistenza nella tua lingua gratuitamente.

Chiamata 800-722-1471 (TTY: 800-842-5357).
Este aviso contiene información importante. Es posible que este aviso contenga información importante acerca de su solicitud de cobertura a través de Premera Blue Cross. Es posible que haya fechas clave en este aviso. Es posible que deba tomar alguna medida antes de determinadas fechas para mantener su cobertura médica o ayuda con los costos. Usted tiene derecho a recibir esta información y ayuda en su idioma sin costo alguno. Llame al 800-722-1471 (TTY: 800-842-5357).