



## FEP Medical Policy Manual

### FEP 7.03.12 Islet Transplantation for Chronic Pancreatitis and Donislecel-jujn for Type 1 Diabetes

**Annual Effective Policy Date: January 1, 2024**

**Original Policy Date: September 2012**

**Related Policies:**

7.03.02 - Allogeneic Pancreas Transplant

## Islet Transplantation for Chronic Pancreatitis and Donislecel-jujn for Type 1 Diabetes

### Description

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

#### OBJECTIVE

The objective of this evidence review is to determine whether autologous pancreas islet transplantation or allogeneic pancreas islet transplantation with donislecel-jujn improves the net health outcome in individuals with chronic pancreatitis or type 1 diabetes.

## POLICY STATEMENT

Autologous pancreas islet transplantation may be considered **medically necessary** as an adjunct to a total or near-total pancreatectomy in individuals with chronic pancreatitis.

Allogeneic islet transplantation using an FDA-approved cellular therapy product (donislecel-jujn [ie, Lantidra]) is considered **investigational** for the treatment of type 1 diabetes.

Islet transplantation with donislecel-jujn is considered **investigational** in all other situations.

## POLICY GUIDELINES

Only adult subjects were enrolled in donislecel-jujn (Lantidra) clinical studies, although clinical studies did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently than younger patients. Risks of donislecel-jujn infusion in pregnancy have not been assessed.

There are risks associated with the infusion procedure and long-term immunosuppression. There is no evidence of donislecel-jujn benefit for individuals whose diabetes is well-controlled with insulin therapy or for those with hypoglycemic unawareness who are able to prevent current repeated severe hypoglycemic events (neuroglycopenia requiring active intervention from a third party) using intensive diabetes management (including insulin, devices, and education).

Repeated intraportal islet infusions are not recommended in patients who have experienced prior portal thrombosis, unless the thrombosis was limited to second- or third-order portal vein branches. There is no evidence to support donislecel-jujn for individuals with liver disease, renal failure, or who have received a renal transplant.

Islet transplantation does not supplant future whole pancreatic transplantation (see policy 7.03.02).

A specific target of HbA1c cannot be provided for all patients, as the target can be different based on age, duration of diabetes, and diabetic complications.

"Current repeated episodes" indicates risk within 1 year of the intended transplantation and is not related to events more than 1 year prior to the intended transplantation.

## BENEFIT APPLICATION

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

Islet transplantation is a specialized procedure that may require referral to an out-of-network facility.

## FDA REGULATORY STATUS

The U.S. Food and Drug Administration (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. Allogeneic islet cells are included in these regulations. Donislecel-jujn (Lantidra™), a first-in-class deceased donor-derived allogeneic pancreatic islet cellular therapy product, was approved by the FDA in June 2023 for the treatment of type 1 diabetes in adults who are unable to approach target hemoglobin A1c due to repeated episodes of severe hypoglycemia despite intensive diabetes management and education.<sup>3</sup>

## RATIONALE

### Summary of Evidence

For individuals with chronic pancreatitis undergoing total or near-total pancreatectomy who receive autologous pancreas islet transplantation, the evidence includes nonrandomized studies and systematic reviews. Relevant outcomes are overall survival (OS), 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 from chronic pancreatitis. The procedure appears to decrease significantly 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 an improvement in the net health outcome.

For individuals with type 1 diabetes who receive allogeneic pancreas islet transplantation with donislecel-jujn, the evidence includes single-arm prospective trials conducted at a single study site without strict protocols demonstrating insulin independence for over 1 year in a majority of participants, with mean insulin independence of approximately 5 years, resulting in Food and Drug Administration approval of donislecel for adults who are unable to approach target HbA1c because of current repeated episodes of severe hypoglycemia despite intensive diabetes management and education and for use in conjunction with concomitant immunosuppression. Additional well-designed studies are required to determine the effects of allogeneic islet transplantation in patients with type 1 diabetes. The evidence is insufficient 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.

#### National Institute for Health and Care Excellence

In 2008, NICE published guidance indicating 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 risk of adverse events.<sup>51</sup> 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)."<sup>52</sup>

#### American Diabetes Association

In 2023, the American Diabetes Association standards of medical care recommended autologous islet cell transplantation be considered in patients undergoing total pancreatectomy for chronic pancreatitis to prevent postsurgical diabetes.<sup>53</sup> The standards of care note that islet cell transplantation may have a role in type 1 diabetes. Because of the need for immunosuppressive agents posttransplantation, the guidelines note that transplantation in type 1 diabetes should be reserved for patients also undergoing renal transplantation or experiencing recurrent ketoacidosis with severe hypoglycemia despite intensive management.

#### International Consensus Guidelines for Chronic Pancreatitis

In 2020, the International Consensus Guidelines for Chronic Pancreatitis panel released a statement on the role of total pancreatectomy and islet transplant in patients with chronic pancreatitis.<sup>54</sup> The panel stated that islet transplant should be considered for patients undergoing total pancreatectomy due to the potential for insulin independence and better long-term glycemic outcomes compared to pancreatectomy alone (weak recommendation based on low quality evidence). However, there is not enough information to definitively conclude when transplant should be performed relative to other interventions. Major indications for pancreatectomy with islet transplant include debilitating pain or recurrent pancreatitis episodes that diminish quality of life (strong recommendation based on low quality evidence). Contraindications to pancreatectomy with islet transplant include active alcoholism, pancreatic cancer, end-stage systemic illness, or psychiatric illness or socioeconomic status that would hinder either the

procedure itself or posttransplant care (strong recommendation based on low quality evidence). Pancreatectomy with islet transplant improves quality of life, opioid use, and pancreatic pain in this population, but evidence about the effect on healthcare utilization is limited.

## U.S. Preventive Services Task Force Recommendations

Not applicable.

## 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.<sup>55</sup> Partial pancreatic tissue transplantation or islet transplantation performed outside a clinical trial are not covered.

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

<b>Date</b>	<b>Action</b>	<b>Description</b>
September 2012	New policy	
March 2013	Replace policy	Policy updated with literature review; policy statement unchanged.
September 2013	Replace policy	Policy updated with literature review; references added; policy statements unchanged.
September 2014	Replace policy	Policy updated with literature review. Reference 4 added. No change in policy statement.
September 2015	Replace policy	Policy updated with literature review; references 1, 3, 6, and 11 added. Policy statements unchanged.
December 2017	Replace policy	Policy updated with literature review through June 22, 2017; Policy statements unchanged.
December 2018	Replace policy	Policy updated with literature review through June 21, 2018; references 1 and 10 added. Policy statements unchanged.
December 2019	Replace policy	Policy updated with literature review through June 10, 2019; no references added, some references removed. Policy statements unchanged.
December 2020	Replace policy	Policy updated with literature review through June 9, 2020; references added. Policy statements unchanged.
December 2021	Replace policy	Policy updated with literature review through June 22, 2021; references added. Policy statements unchanged.
December 2022	Replace policy	Policy updated with literature review through June 17, 2022; references added. Minor editorial refinements to policy statement; intent unchanged.
December 2023	Replace policy	Policy updated with literature review through June 30, 2023; references added. Policy title updated and investigational statement added for use of donislecel-jujn in type 1 diabetes.

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