Molina Clinical Policy
Pancreatic Islet Cell Transplantation (Autologous): Policy No. 440

Last Approval: 8/9/2023
Next Review Due By: August 2024

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Pancreatitis is a condition in which digestive enzymes become activated while still in pancreas, causing inflammation in the pancreatic tissue. The most common signs and symptoms are epigastric pain, nausea, and vomiting. Episodes may occur in isolation (acute pancreatitis) or become recurring in nature (chronic pancreatitis). In chronic pancreatitis, pancreatic tissue becomes increasingly damaged. Symptoms may include weight loss, diarrhea, and chronic pain; or infrequently, individuals may be asymptomatic. Long term complications can occur including, but not limited to, diabetes mellitus and bleeding. For those with chronic pancreatitis experiencing intractable pain, total pancreatectomy may be performed, potentially in conjunction with pancreatic islet cell autologous transplantation (Freedman & Forsmark 2023).

Pancreatic islet cell transplantation is a treatment used to preserve normal insulin function in select patients undergoing a total pancreatectomy, near-total pancreatectomy, or completion pancreatectomy for chronic pancreatitis. It has also been proposed as a treatment option for select patients with type I diabetes using islet cells from a living or deceased donor. During islet cell transplantation, special enzymes are employed to remove islets from a resected pancreas. The islets are then purified and counted, diluted in plasma, and finally infused into the portal vein of the liver of the recipient. The types of islet transplant are autologous (self-donor), allogenic (human donor other than self or cadaver), or xenogeneic (animal source). Autologous islet cell transplantation is currently the only accepted of these, with others remaining experimental. There is no immunosuppression required following autologous islet cell transplantation because the donor and recipient are the same. The main contraindication is malignancy of the pancreas (Kluger & Chabot 2021; Robertson & Rickels 2023).

In 2009, the FDA released guidance compiled using data obtained during investigational new drug (IND) studies to aid in the development of products that could be used in allogeneic islet cell transplant. To this date, however, there is no allogeneic islet cell transplant product licensed for use by the FDA.

RELATED POLICIES

MCP-441: Pancreatic Cellular Replacement Therapy Lantidra (donislecel-jujn)

COVERAGE POLICY

Autologous Pancreatic Islet Cell Transplantation may be considered medically necessary as an adjunct to a total or near total pancreatectomy in patients with chronic pancreatitis.

Limitations and Exclusions

Any of the following **are considered experimental, investigational, and unproven** due to insufficient evidence in the peer reviewed published literature:

1. Xenotransplantation

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

Results of the peer reviewed published studies suggest that autologous islet cell transplantation may provide durable improvements in patient-reported pain, reduce narcotic use, provide adequate glycemic control and insulin independence in many patients, improve quality of life in patients with intractable and debilitating symptoms from chronic pancreatitis, and improve survival with an acceptable level of mortality. Several systematic reviews of the literature on islet auto-transplantation (IAT) after total pancreatectomy (TP) or partial pancreatectomy (PP) have been published. A summary of the most relevant publications is outlined below.

Kempeneers et al. (2019) identified 15 observational studies with a total of 1255 individuals who had chronic pancreatitis who underwent total pancreatectomy with islet autotransplant. The pooled 30-day mortality rate was 2% and the 1-year mortality rate was 4%. Four studies assessed the insulin-free rate at 1 year and the other 11 studies reported the insulin-free rate at last follow-up. In pooled analyses, the insulin-free rate at 1 year was 30% (95% confidence interval [CI], 20-43%) and at last follow-up the insulin-free event rate was 1.31 (95% CI, 0.74 to 2.31) per 10 person-years. In the 5 studies that reported this outcome, pain assessed by a 100-point visual analogue scale (VAS) decreased by a mean of 58 points (from a preoperative mean of 79 to a post-operative mean of 22). In 6 studies, the pooled 1-year opioid-free rate was 63% (95% CI, 46-77%).

Wu et al. (2015) performed a systematic review and meta-analysis evaluating outcomes of IAT after TP. A total of 12 studies with a total of 677 subjects were included. The insulin independent rate for IAT after TP at last follow-up was 3.72 per 100 person-years (95% CI, 1.00-6.44). The 30-day mortality was 2.1% (95% CI, 1.2-3.8%). The mortality at last follow-up was 1.09 per 100 person-years (95% CI, 0.21-1.97). Factors associated with incidence density of insulin independence in univariate meta-regression analyses included islet equivalents per kg body weight.

Sutherland et al. (2012) reported data from a single center series of 409 individuals with chronic pancreatitis who were treated between 1977 and 2011 with TP and IAT to relieve pain and preserve β-cell mass. Fifty-three of the 409 participants (13%) were children between the ages of 5 and 18 years. Post TP and IAT actuarial survival at 1 year was 96% in adults and 98% in children, and 5-year survival was 89% in adults and 98% in children. Overall, at 15 years post-surgery, two-thirds (66%) of the individuals were reported alive. Insulin independence at 3 years was noted in 30% of individuals (25% of adults and 55% of children), while partial function was reported in 33%. Surgical complications requiring reoperation during the initial admission occurred in a total of 15.9% of the individuals, with bleeding as the most common reason for reoperation experienced in 9.5%. There was a total of 5 (1.2%) in-hospital deaths, and 53 deaths following initial discharge with 3 of those deaths related to chronic pancreatitis disease processes. Insulin independence at 6 months was observed in 25% of individuals, 33% had partial islet function and less than one-fifth were dependent on insulin. Narcotic use for pain control declined after TP and IAT. The proportion of individuals requiring narcotics were, 91%, 61%, 54% and 51% at 3, 6, 12 and 24 months, respectively. A survey of integrated quality-of-life outcomes showed that at 1 year of the 191 participants, 85% reported improvement compared to the prior year. The authors concluded TP alleviates pain caused by chronic pancreatitis and IAT can help to preserve glycemic control in most individuals.

The **American Diabetes Association** (2022) *Standards of Medical Care in Diabetes* which recommends that islet auto-transplantation should be considered for patients requiring total pancreatectomy for medically refractory chronic pancreatitis to prevent postsurgical diabetes. The standards state that approximately one-third of patients undergoing total pancreatectomy with islet auto-transplantation are insulin free 1 year postoperatively, and observational studies from different centers have demonstrated islet graft function up to a decade after the surgery in some patients. Both patient and disease factors should be carefully considered when deciding the indications and timing of this surgery. Surgeries should be performed in skilled facilities that have demonstrated expertise in islet auto-transplantation.

SUPPLEMENTAL INFORMATION

None.

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology) Codes

CPT	Description
0584T	Islet cell transplant, includes portal vein catheterization and infusion, including all imaging, including guidance, and radiological supervision and interpretation, when performed; percutaneous
0585T	Islet cell transplant, includes portal vein catheterization and infusion, including all imaging, including guidance, and radiological supervision and interpretation, when performed; laparoscopic
0586T	Islet cell transplant, includes portal vein catheterization and infusion, including all imaging, including guidance, and radiological supervision and interpretation, when performed; open
48160	Pancreatectomy, total or subtotal, with autologous transplantation of pancreas or pancreatic islet cells

HCPCS (Healthcare Common Procedure Coding System) Code

HCPCS	Description
G0341	Percutaneous islet cell transplant, includes portal vein catheterization and infusion
G0342	Laparoscopy for islet cell transplant, includes portal vein catheterization and infusion
G0343	Laparotomy for islet cell transplant, includes portal vein catheterization and infusion

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

08/09/2023 Allogenic transplantation information removed from policy. Added cross-reference to new MCP on allogenic islet cell transplantation in the related policies section.

06/14/2023 Policy separated from original policy "Pancreas Transplant Procedures." Overview, Summary of Medicaid Evidence, and references updated. No changes to criteria. Policy reviewed in May 2023 by an Advanced Medical Reviews (AMR) practicing, board-certified physician in the areas of Surgery, Transplant.

06/08/2022 Policy reviewed, no changes to criteria; included section on marijuana use; updated Overview, Summary of Medical Evidence, and Reference sections.

06/09/2021 Policy reviewed, updated references. Added CPT codes: 48551, 48552, 50323, 50325, 50327.

04/23/2020 Policy updated with medically necessary criteria for autologous pancreatic islet cell transplantation when used as an adjunct to a total or near total pancreatectomy in patients with chronic pancreatitis. Updated references, guidelines; added three new 2020 CPT codes (0584T, 0585T, 0586T) and one new ICD-10 code (K86.0-K86.1) for chronic pancreatitis. Policy reviewed in January 2020 by an Advanced Medical Reviews (AMR) practicing, board-certified physician in the areas of Surgery, Transplant.

REFERENCES

1. Centers for Medicare and Medicaid Services (CMS). Medicare coverage database: National coverage determination – islet cell transplantation in the context of a clinical trial (260.3.1). Effective October 1, 2004. https://www.cms.gov/medicare-coverage-database/search.aspx
2. Food and Drug Administration (FDA). Guidance document: Considerations for allogeneic pancreatic islet cell products (guidance for industry). Published September 2009. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-allogeneic-pancreatic-islet-cell-products
3. American Diabetes Association Professional Practice Committee. 4. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Medical Care in Diabetes-2022. Diabetes Care. 2022 Jan 1;45(Suppl 1):S46-S59. doi: 10.2337/dc22-S004. PMID: 34964869; PMCID: PMC8935396.

4. Organ Procurement and Transplantation Network (OPTN). Guidance. https://optn.transplant.hrsa.gov/professionals/by-topic/guidance/.
5. Robertson RP, Davis C, Larsen J, et al.; American Diabetes Association (ADA). Pancreas and islet transplantation in type 1 diabetes. Diabetes Care. 2006 Apr;29(4):935. doi: 10.2337/diacare.29.04.06.dc06-9908. PMID: 16567844.
6. United Network for Organ Sharing (UNOS). About UNOS. https://unos.org/about/.
7. Kempeneers MA, Scholten L, Verkade CR, et al. Efficacy of total pancreatectomy with islet auto-transplantation on opioid and insulin requirement in painful chronic pancreatitis: A systematic review and meta-analysis. Surgery. 2019 Sep;166(3):263-270. doi: 10.1016/j.surg.2019.03.014.
8. Sutherland DER, Radosevich DM, Bellin MD, et al. Total pancreatectomy and islet auto-transplantation for chronic pancreatitis. J Am Coll Surg. 2012 Apr;214(4):409-24; discussion 424-6. doi: 10.1016/j.jamcollsurg.2011.12.040.
9. Wu Q, Zhang M, Qin Y, et al. Systematic review and meta-analysis of islet auto-transplantation after total pancreatectomy in chronic pancreatitis patients. Endocr J. 2015;62(3):227-34. doi: 10.1507/endocrj.EJ14-0510.
10. Zhang YJ, Duan DD, Yuan H. Efficacy and safety of islet auto-transplantation after total pancreatectomy in chronic pancreatitis: A systematic review and meta-analysis including 17 studies. Clin Res Hepatol Gastroenterol. 2020 Sep;44(4):598-608. doi: 10.1016/j.clinre.2019.08.004.
11. Alhamad T, Stratta RJ. Pancreas-kidney transplantation in diabetes mellitus: Patient selection and pretransplant evaluation. Updated Jan 19, 2023. https://www.uptodate.com/.
12. Bloom RD. Kidney function and non-kidney solid organ transplantation. Updated July 9, 2021. https://www.uptodate.com/.
13. [1] DynaMed. Management of type 1 diabetes. https://www.dynamed.com/management/management-of-type-1-diabetes
14. [2] DynaMed. Pancreas transplant. https://www.dynamed.com/procedure/pancreas-transplant
15. Freedman SD, Forsmark CE. Chronic pancreatitis: Clinical manifestations and diagnosis in adults. Updated February 21, 2023. https://www.uptodate.com/.
16. Kluger MD, Chabot J. Total Pancreatectomy. Updated July 28, 2021. https://www.uptodate.com/.
17. Robertson RP, Rickels MR. Pancreas and islet transplantation in diabetes mellitus. Updated April 10, 2023. https://www.uptodate.com/.
18. Bellin MD, Beilman GJ, Dunn TB, et al. Sitagliptin treatment after total pancreatectomy with islet auto-transplantation: A randomized, placebo-controlled study. Am J Transplant. 2017 Feb;17(2):443-450. doi: 10.1111/ajt.13979.
19. Boggi U, Vistoli F, Andres A, et al. First World Consensus Conference on pancreas transplantation: Part II - recommendations. Am J Transplant. 2021 Sep;21 Suppl 3(Suppl 3):17-59. doi: 10.1111/ajt.16750. Epub 2021 Jul 29. PMID: 34245223; PMCID: PMC8518376.
20. Colling KP, Bellin MD, Schwarzenberg SJ, et al. Total pancreatectomy with intraportal islet auto-transplantation as a treatment of chronic pancreatitis in patients with CFTR mutations. Pancreas. 2018 Feb;47(2):238-244. doi: 10.1097/MPA.0000000000000968.
21. Fazlalizadeh R, Moghadamyeghaneh Z, Demirjian AN, et al. Total pancreatectomy and islet auto-transplantation: A decade nationwide analysis. World J Transplant. 2016 Mar 24;6(1):233-8. doi: 10.5500/wjt. v6.i1.233.
22. Health Quality Ontario. Pancreas Islet Transplantation for Patients with Type 1 Diabetes Mellitus: A Clinical Evidence Review. Ont Health Technol Assess Ser. 2015 Sep 1;15(16):1-84. PMID: 26644812; PMCID: PMC4664938.
23. Kesseli SJ, Wagar M, Jung MK, et al. Long-term glycemic control in adult patients undergoing remote vs. local total pancreatectomy with islet auto-transplantation. Am J Gastroenterol. 2017 Apr;112(4):643-649. doi: 10.1038/ajg.2017.14.
24. Kizilgul M, Wilhelm JJ, Beilman GJ, et al. Effect of intrapancreatic fat on diabetes outcomes after total pancreatectomy with islet auto-transplantation. J Diabetes. 2018 Apr;10(4):286-295. doi: 10.1111/1753-0407.12589.
25. Lane A, Hodges JS, Ptacek P, et al. Low prevalence of diabetes distress following total pancreatectomy with islet auto-transplantation. Clin Transplant. 2018 May;32(5):e13237. doi: 10.1111/ctr.13237.
26. Maffi P, Nano R, Monti P, et al. Islet allotransplantation in the bone marrow of patients with type 1 diabetes: A pilot randomized trial. Transplantation. 2019 Apr;103(4):839-851. doi: 10.1097/TP.0000000000002416.
27. Morgan KA, Lancaster WP, Owczarski SM. Patient selection for total pancreatectomy with islet auto-transplantation in the surgical management of chronic pancreatitis. J Am Coll Surg. 2018 Apr;226(4):446-451. doi: 10.1016/j.jamcollsurg.2017.12.018.
28. Roll GR, Posselt AM, Freise J, et al. Long-term follow-up of beta cell replacement therapy in 10 HIV-infected patients with renal failure secondary to type 1 diabetes mellitus. Am J Transplant. 2020 Aug;20(8):2091-2100. doi: 10.1111/ajt.15796. Epub 2020 Feb 28. PMID: 31994295; PMCID: PMC7650842.
29. Shahbazov R, Naziruddin B, Salam O. et al. The impact of surgical complications on the outcome of total pancreatectomy with islet auto-transplantation. Am J Surg. 2020 Jan;219(1):99-105. doi: 10.1016/j.amjsurg.2019.04.007.
30. Wilson GC, Sutton JM, Abbott DE, et al. Long-term outcomes after total pancreatectomy and islet cell auto-transplantation: Is it a durable operation? Ann Surg. 2014 Oct;260(4):659-65; discussion 665-7. doi: 10.1097/SLA.0000000000000920.
31. Wilson GC, Sutton JM, Smith MT, et al. Completion pancreatectomy and islet cell auto-transplantation as salvage therapy for patients failing previous operative interventions for chronic pancreatitis. Surgery. 2015 Oct;158(4):872-8; discussion 879-80. doi: 10.1016/j.surg.2015.04.045.
32. Wilson GC, Sutton JM, Smith MT, et al. Total pancreatectomy with islet cell auto-transplantation as the initial treatment for minimal-change chronic pancreatitis. HPB (Oxford). 2015 Mar;17(3):232-8. doi: 10.1111/hpb.12341.