

(70305)

<b>Medical Benefit</b>		<b>Effective Date:</b> 07/01/14	<b>Next Review Date:</b> 05/21
<b>Preauthorization</b>	Yes	<b>Review Dates:</b> 05/09, 05/10, 05/11, 05/12, 05/13, 07/13, 05/14, 05/15, 05/16, 05/17, 05/18, 05/19, 05/20	

***Preauthorization is required and must be obtained through Case Management.***

*The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.*

Populations	Interventions	Comparators	Outcomes
Individuals: • With intestinal failure and evidence of impending end-stage liver failure	Interventions of interest are: • Small bowel and liver transplant alone or multivisceral transplant	Comparators of interest are: • Medical management • Parenteral nutrition	Relevant outcomes include: • Overall survival • Morbid events • Treatment-related mortality • Treatment-related morbidity
Individuals: • With a failed small bowel and liver or multivisceral transplant without contraindications for retransplant	Interventions of interest are: • Small bowel and liver retransplant alone or multivisceral retransplant	Comparators of interest are: • Medical management • Parenteral nutrition	Relevant outcomes include: • Overall survival • Morbid events • Treatment-related mortality • Treatment-related morbidity

### DESCRIPTION

This protocol addresses transplantation and retransplantation of an intestinal allograft in combination with a liver allograft, either alone or in combination with one or more of the following organs: stomach, duodenum, jejunum, ileum, pancreas, or colon.

### SUMMARY OF EVIDENCE

For individuals who have intestinal failure and evidence of impending end-stage liver failure who receive a small bowel and liver transplant alone or multivisceral transplant, the evidence includes a limited number of case series. The relevant outcomes are overall survival, morbid events, and treatment-related mortality and morbidity. These transplant procedures are infrequently performed and few reported case series exist. However, results from the available case series have revealed fairly high postprocedural survival rates. Given these results and the exceedingly poor survival rates of patients who exhaust all other treatments, transplantation may prove not only to be the last option but also a beneficial one. Transplantation is contraindicated for patients in whom the procedure is expected to be futile due to comorbid disease, or in whom posttransplantation care is expected to significantly worsen comorbid conditions. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have a failed small bowel and liver or multivisceral transplant without contraindications for retransplant who receive a small bowel and liver retransplant alone or multivisceral retransplant, the evidence includes case series. The relevant outcomes are overall survival, morbid events, and treatment-related mortality and morbidity. Although limited in quantity, the available post retransplantation data have suggested reasonably high survival rates. Given exceedingly poor survival rates without retransplantation of patients who have exhausted other treatments, evidence of postoperative survival from uncontrolled studies is sufficient to demonstrate that retransplantation provides a survival benefit in appropriately selected patients. Retransplantation is contraindicated for patients in whom the procedure is expected to be futile due to comorbid disease or in whom posttransplantation care is expected to significantly worsen comorbid conditions. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

## POLICY

Transplants, such as a multivisceral transplant and a small bowel and liver transplant, may be considered **medically necessary** for pediatric and adult patients with intestinal failure (characterized by loss of absorption and the inability to maintain protein-energy, fluid, electrolyte, or micronutrient balance), who have been managed with long-term total parenteral nutrition and who have developed evidence of impending end-stage liver failure.

Retransplants, such as a multivisceral retransplant and a small bowel and liver retransplant, may be considered **medically necessary** after a failed primary small bowel and liver transplant or multivisceral transplant.

A small bowel and liver transplant or multivisceral transplant is considered **investigational** in all other situations.

## POLICY GUIDELINES

### GENERAL

Individual transplant facilities may have their own additional requirements or protocols that must be met in order for the patient to be eligible for a transplant at their facility.

Potential contraindications to solid organ transplant are subject to the judgment of the transplant center and include the following:

1. Known current malignancy, including metastatic cancer
2. Recent malignancy with high risk of recurrence
3. History of cancer with a moderate risk of recurrence
4. Systemic disease that could be exacerbated by immunosuppression
5. Untreated systemic infection making immunosuppression unsafe, including chronic infection
6. Other irreversible end-stage disease not attributed to intestinal failure
7. Psychosocial conditions or chemical dependency affecting ability to adhere to therapy.

Intestinal failure results from surgical resection, congenital defect, or disease-associated loss of absorption and is characterized by the inability to maintain protein-energy, fluid, electrolyte, or micronutrient balance. Short-bowel syndrome is one case of intestinal failure.

Candidates should meet the following criteria:

- Adequate cardiopulmonary status
- Documentation of patient compliance with medical management.

## SMALL BOWEL/LIVER SPECIFIC CRITERIA

Evidence of intolerance of total parenteral nutrition (TPN) includes, but is not limited to, multiple and prolonged hospitalizations to treat TPN-related complications, or the development of progressive but reversible liver failure. In the setting of progressive liver failure, small bowel transplant may be considered a technique to avoid end-stage liver failure related to chronic TPN, thus avoiding the necessity of a multivisceral transplant.

## MEDICARE ADVANTAGE

If a transplant is needed, we arrange to have the Medicare–approved transplant center review and decide whether the patient is an appropriate candidate for the transplant.

## BACKGROUND

### SHORT BOWEL SYNDROME

Short bowel syndrome is defined as an inadequate absorbing surface of the small intestine due to extensive disease or surgical removal of a large portion of the small intestine. In some instances, short bowel syndrome is associated with liver failure, often due to the long-term complications of total parenteral nutrition.

### Treatment

A small bowel/liver transplant or a multivisceral transplant includes the small bowel and liver with one or more of the following organs: stomach, duodenum, jejunum, ileum, pancreas, and/or colon. The type of transplantation depends on the underlying etiology of intestinal failure, quality of native organs, presence or severity of liver disease, and history of prior abdominal surgeries.<sup>1</sup> A multivisceral transplant is indicated when anatomic or other medical problems preclude a small bowel/liver transplant. Complications following small bowel/liver and multivisceral transplants include acute or chronic rejection, donor-specific antibodies, infection, lymphoproliferative disorder, graft-versus-host disease, and renal dysfunction.<sup>2</sup>

## REGULATORY STATUS

Small bowel/liver and multivisceral transplantation are surgical procedures and, as such, are not subject to regulation by the U.S. Food and Drug Administration.

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. Pancreas transplants are included in these regulations.

## RELATED PROTOCOL

Isolated Small Bowel Transplant

---

Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary Services Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

## REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

1. Bharadwaj S, Tandon P, Gohel TD, et al. Current status of intestinal and multivisceral transplantation. *Gastroenterol Rep (Oxf)*. Feb 2017;5(1):20-28. PMID 28130374.
2. Loo L, Vrakas G, Reddy S, et al. Intestinal transplantation: a review. *Curr Opin Gastroenterol*. May 2017; 33(3):203-211. PMID 28282321.
3. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Small bowel transplants in adults and multivisceral transplants in adults and children. *TEC Assessments*. 1999;Volume 14:Tab 9.
4. Mangus RS, Tector AJ, Kubal CA, et al. Multivisceral transplantation: expanding indications and improving outcomes. *J Gastrointest Surg*. Jan 2013;17(1):179-186; discussion p 186-177. PMID 23070622.
5. Abu-Elmagd KM, Costa G, Bond GJ, et al. Five hundred intestinal and multivisceral transplantations at a single center: major advances with new challenges. *Ann Surg*. Oct 2009;250(4):567-581. PMID 19730240.
6. Desai CS, Khan KM, Gruessner AC, et al. Intestinal retransplantation: analysis of Organ Procurement and Transplantation Network database. *Transplantation*. Jan 15 2012;93(1):120-125. PMID 22113492.
7. Lacaille F, Irtan S, Dupic L, et al. Twenty-eight years of intestinal transplantation in Paris: experience of the oldest European center. *Transpl Int*. Feb 2017;30(2):178-186. PMID 27889929.
8. Garcia Aroz S, Tzvetanov I, Hetterman EA, et al. Long-term outcomes of living-related small intestinal transplantation in children: A single-center experience. *Pediatr Transplant*. Jun 2017;21(4). PMID 28295952.
9. Dore M, Junco PT, Andres AM, et al. Surgical rehabilitation techniques in children with poor prognosis short bowel syndrome. *Eur J Pediatr Surg*. Feb 2016;26(1):112-116. PMID 26535775.
10. Rutter CS, Amin I, Russell NK, et al. Adult intestinal and multivisceral transplantation: experience from a single center in the United Kingdom. *Transplant Proc*. Mar 2016;48(2):468-472. PMID 27109980.
11. Lauro A, Zanfi C, Dazzi A, et al. Disease-related intestinal transplant in adults: results from a single center. *Transplant Proc*. Jan-Feb 2014;46(1):245-248. PMID 24507060.
12. Varkey J, Simren M, Bosaeus I, et al. Survival of patients evaluated for intestinal and multivisceral transplantation - the Scandinavian experience. *Scand J Gastroenterol*. Jun 2013;48(6):702-711. PMID 23544434.
13. Nagai S, Mangus RS, Anderson E, et al. Cytomegalovirus infection after intestinal/multivisceral transplantation: a single-center experience with 210 cases. *Transplantation*. Feb 2016;100(2):451-460. PMID 26247555.
14. Timpone JG, Yimen M, Cox S, et al. Resistant cytomegalovirus in intestinal and multivisceral transplant recipients. *Transpl Infect Dis*. Apr 2016;18(2):202-209. PMID 26853894.
15. Wu GS, Cruz RJ, Jr., Cai JC. Acute antibody-mediated rejection after intestinal transplantation. *World J Transplant*. Dec 24 2016;6(4):719-728. PMID 28058223.
16. Cromvik J, Varkey J, Herlenius G, et al. Graft-versus-host disease after intestinal or multivisceral transplantation: a Scandinavian single-center experience. *Transplant Proc*. Jan-Feb 2016;48(1):185-190. PMID 26915866.
17. Florescu DF, Qiu F, Langnas AN, et al. Bloodstream infections during the first year after pediatric small bowel transplantation. *Pediatr Infect Dis J*. Mar 29 2012;31(7):700-704. PMID 22466325.
18. Wu G, Selvaggi G, Nishida S, et al. Graft-versus-host disease after intestinal and multivisceral transplantation. *Transplantation*. Jan 27 2011;91(2):219-224. PMID 21076376.
19. Organ Procurement and Transplantation Network (OPTN). Organ Procurement and Transplantation Network Policies. 2018; [https://optn.transplant.hrsa.gov/media/1200/optn\\_policies.pdf](https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf). Accessed August 29, 2019.

20. Working Party of the British Transplantation Society. Kidney and Pancreas Transplantation in Patients with HIV. Second Edition (Revised). British Transplantation Society Guidelines. Macclesfield, UK: British Transplantation Society; 2017.
21. Ekser B, Kubal CA, Fridell JA, et al. Comparable outcomes in intestinal retransplantation: Single-center cohort study. *Clin Transplant*. May 21 2018:e13290. PMID 29782661.
22. Mazariegos GV, Soltys K, Bond G, et al. Pediatric intestinal retransplantation: techniques, management, and outcomes. *Transplantation*. Dec 27 2008;86(12):1777-1782. PMID 19104421.
23. American Gastroenterological Association (AGA). American Gastroenterological Association medical position statement: short bowel syndrome and intestinal transplantation. *Gastroenterology*. Apr 2003;124(4):1105-1110. PMID 12671903.
24. Kaufman SS, Atkinson JB, Bianchi A, et al. Indications for pediatric intestinal transplantation: a position paper of the American Society of Transplantation. *Pediatr Transplant*. Apr 2001;5(2):80-87. PMID 11328544.
25. Center for Medicare & Medicaid Services. National Coverage Determination (NCD) for Intestinal and Multi-Visceral Transplantation (260.5). 2006; <https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=280&ncdver=2&CoverageSelection=National&Keyword=intestinal&KeywordLookup=Title&KeywordSearchType=And&generalError=Thank+you+for+your+interest+in+the+Medicare+Coverage+Database.+You+may+only+view+the+page+you+attempted+to+access+via+normal+usage+of+the+Medicare+Coverage+Database.&bc=gAAAACAAAAAAA%3d%3d&>. Accessed August 29, 2019.