Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 1/1/24**
(See policy history boxes for previous effective dates)

Title: Small Bowel/Liver and Multivisceral Transplant

Description/Background

Solid organ transplantation offers a treatment option for patients with different types of end-stage organ failure that can be lifesaving or provide significant improvements to a patient's quality of life.[1] Many advances have been made in the last several decades to reduce perioperative complications. Available data supports improvement in long-term survival as well as improved quality of life, particularly for liver, kidney, pancreas, heart, and lung transplants. Allograft rejection remains a key early and late complication risk for any organ transplantation. Transplant recipients require life-long immunosuppression to prevent rejection. Patients are prioritized for transplant by mortality risk and severity of illness criteria developed by Organ Procurement and Transplantation Network and United Network of Organ Sharing.

Small Bowel/Liver and Multivisceral Transplant

In 2022, 42,889transplants were performed in the United States procured from almost 36,421 deceased donors and 6,468 living donors.[2] Intestinal transplants occur less frequently than other organ transplants, with 10 or fewer patients receiving liver-intestine transplant each year from 2008 to 2019. Small bowel and liver or multivisceral transplant is usually considered in adults and children who develop serious complications related to parenteral nutrition, including inaccessibility (e.g., due to thrombosis) of access sites, catheter-related sepsis, and cholestatic liver disease.

SHORT BOWEL SYNDROME

Small bowel transplants are typically performed in patients with short bowel syndrome, defined as an inadequate absorbing surface of the small intestine due to extensive disease or surgical removal of a large portion of small intestine.[3] In some instances, short bowel syndrome is associated with liver failure, often due to the long-term complications of total parenteral nutrition (TPN).

Treatment
These patients may be candidates for a small bowel/liver transplant or a multivisceral transplant, which includes the small bowel and liver with 1 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.[4] 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.[5]

Modified Multivisceral Transplantation
A full multivisceral transplantation involves the en bloc transplantation of the stomach, liver, duodenum and pancreas with the intestine. In a modified procedure only one or two organs may be transplanted. It is indicated for patients with irreversible failure of their abdominal visceral organs, including the small bowel.

Medical Policy Statement

The safety and effectiveness of a small bowel/liver and/or multivisceral transplant have been established. It may be considered a useful therapeutic option when indicated in adult and pediatric individuals 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 (TPN) and who have developed evidence of impending end-stage liver failure.

A small bowel/liver transplant or multivisceral retransplant may be considered established for individuals following a failed primary small bowel/liver transplant or multivisceral transplant.

A modified multivisceral transplantation may be considered established for individuals requiring only one or two organs (e.g. stomach, liver, duodenum, pancreas, intestine) to be transplanted.

A small bowel/liver transplant or multivisceral transplant is considered experimental/ investigational in all other situations.

Inclusionary and Exclusionary Guidelines

Inclusions:
The individual selected for small bowel/liver, small/bowel multivisceral transplant and/or modified multivisceral transplant must meet the transplanting institution's protocol eligibility criteria. These criteria should include:
- Documentation of patient compliance with medical management
- Adequate cardiopulmonary status

HIV [human immunodeficiency virus]-positive individuals who meet the following criteria, as stated in the 2001 guidelines of the American Society of Transplantation, could be considered candidates for small bowel/liver or multivisceral transplantation:
- CD4 count greater than 200 cells per cubic millimeter for greater than 6 months

- HIV-1 RNA undetectable
- On stable anti-retroviral therapy >3 months
- No other complications from AIDS [acquired immune deficiency syndrome] (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidiosis mycosis, resistant fungal infections, Kaposi's sarcoma, or other neoplasm), and meeting all other criteria for transplantation.

Exclusions:
Potential contraindications to solid organ transplant are subject to the judgment of the transplant center:
- Known current malignancy, including metastatic cancer
- Recent malignancy with high risk of recurrence
- History of cancer with a moderate risk of recurrence
- Systemic disease that could be exacerbated by immunosuppression
- Untreated systemic infection making immunosuppression unsafe, including chronic infection
- Other irreversible end-stage disease not attributed to intestinal failure
- Psychosocial conditions or chemical dependency affecting ability to adhere to therapy

Small Bowel/Liver Specific

Inclusions
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.

Contraindications
Absolute and relative contraindications represent situations where proceeding with transplant may not be advisable in the context of limited organ/tissue availability. Contraindications may evolve over time as transplant experience grows in the medical community. Clinical documentation supplied to the health plan *must* demonstrate that attending staff at the transplant center have considered *all* contraindications as part of their overall evaluation of potential organ transplant recipients and have decided to proceed.

Relative contraindications:
The selection process for approved organ transplants is designed to obtain the best result for each patient. Therefore, relative contraindications to small bowel/liver or multivisceral transplant may include, but are not limited to:
- Poor cardiac function: Ejection fraction should be greater than 45% with no overt symptoms of congestive heart failure.
- Poor pulmonary function: Pulmonary function tests must be greater than or equal to 50% of predicted value.
- Poor renal function: Renal creatinine clearance should be greater than 40 ml/min or creatinine must be less than or equal to 2mg/dl.
- Poor liver function: There should be no history of severe chronic liver disease
- Presence of uncontrolled HIV or an active form of hepatitis B, hepatitis C or human T-cell lymphotropic virus (HTLV-1).

Note: there is a separate liver transplantation policy

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)*

Established codes:

44120	44121	44132	44133	44135	44136
44715	44720	44721	44799	47133	47135
47399	47140	47141	47142	47143	47144
47145	47146	47147	S2053	S2054	S2055

Other codes (investigational, not medically necessary, etc.):

N/A

Rationale

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

TRANSPLANTATION OF SMALL BOWEL/LIVER OR MULTIVISCERAL ORGANS

Clinical Context and Therapy Purpose

The purpose of small bowel and liver transplant alone or multivisceral transplant in patients who have intestinal failure and evidence of impending end-stage liver failure is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following **PICOs** were used to select literature to inform this review.

Populations
The relevant population of interest is individuals with intestinal failure and evidence of impending end-stage liver failure.

Interventions
The therapy being considered is small bowel and liver transplant alone or multivisceral transplant.

Comparators
The following practices are currently being used to make decisions about intestinal failure and evidence of impending end-stage liver failure: medical management and parenteral nutrition.

Outcomes
The general outcomes of interest are overall survival (OS), morbid events, and treatment-related mortality and morbidity.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Within each category of study design, studies with larger sample sizes and longer duration were preferred.
- Studies with duplicative or overlapping populations were excluded.

Systematic Reviews
A 1999 TEC Assessment focused on multivisceral transplantation and offered the following conclusions: Multivisceral transplantation in patients with small bowel syndrome, liver failure, and/or other gastrointestinal problems such as pancreatic failure, thromboses of the celiac axis and the superior mesenteric artery, or pseudo-obstruction affecting the entire gastrointestinal tract associated with poor patient and graft survival. Pediatric and adult patients have a similar 2- and 5-year survival of 33–50%. However, without this procedure, it is expected that these patients would face 100% mortality.[6]

Registry Studies and Case Series
The published literature consists of a registry study and case series, mainly reported by single centers in the United States and Europe. Tables 1 and 2 summarize the characteristics and results of the publications respectively.

Reasons for transplantations were mainly short bowel syndrome. Other reasons included congenital enteropathies and motility disorders. Most common outcomes reported were survival rates and weaning off total parenteral nutrition (TPN). Several studies have presented survival rates by type of transplantation, while others have combined all types of transplants when reporting survival rates. When rates were reported by type of transplant, isolated transplantations had higher survival rates than multivisceral transplants (see Table 2).

Several investigators have reported higher survival rates in transplants conducted more recently than those conducted earlier.[7-10] Reasons for improved survival rates in more recent years have been attributed to the development of more effective immunosuppressive drugs and the learning curve for the complex procedure.

Authors of these publications, as well as related reviews, have observed that while outcomes have improved over time, recurrent and chronic rejection and complications of immunosuppression continue to be obstacles to long-term survival. A separate discussion of complications follows the evidence tables.

Table 1. Summary of Key Registry Studies and Case Series Characteristics for Transplants

Author (Year)	Location	N	Median Age (Range), Y	Interventions		Follow-up (Range)
				Treatment	**n**	
Raghu et al (2019)	International	2080	2.5 (1.1-6.3)	• Isolated IT • Combined liver IT • Multivisceral Graft (including modified [intestine and stomach without liver] and full [intestine, stomach, and liver])	725 966 389	5 y
Lacaille et al (2017)	France	110	5.3 (0.4-19)	• Isolated IT • Combined liver IT • Multivisceral graft	45 60 5	Of 55 alive: • 17 at <5 y • 17 at 5-10 y • 21 at ≥10 y
Garcia Aroz et al (2017)	United States	10	1.5 (0.7-13)	• Isolated IT • Combined liver IT	7 3	6/7 alive at follow-up ≥ 10 y
Dore et al (2016)	United States	30	0.2 (0.1-18)	• Isolated IT • Combined liver IT • Multivisceral graft	6 6 18	28 (4-175) mo
Rutter et al (2016)	United Kingdom	60	1.8 (0-8)	• Isolated IT • Multivisceral graft • Modified multivisceral	16 35 9	21.3 (0-95) mo
Lauro et al (2014)	Italy	46	34 (NR)	• Isolated IT • Combined liver IT • Multivisceral graft	34 6 6	51.3 mo
Varkey et al (2013)	Sweden	20	Adults: 44 (20-67) Children: 6 (0.5-13)	• Isolated IT • Combined liver IT • Multivisceral graft	4 1 15	NR
Mangus et al (2013)	United States	100	Adults: 48 (NR to 66) Children: 1 (0.6 to NR)	• Multivisceral graft • Modified multivisceral	84 16	25 mo

IT: intestinal transplantation; NR: not reported.
[a] Living donors

Table 2. Summary of Key Case Series Results for Transplantations

Author	Interventions	Survival	Off TPN

(Year)				
	Treatment	**n**		
Raghu et al (2019)	• Isolated It • Combined liver IT • Multivisceral graft (including modified [intestine and stomach without liver] and full [intestine, stomach, and liver])	725 966 389	All transplantations combined: • Patient survival: 72.7% at 1 y; 57.2% at 5 y • Graft survival: 66.1% at 1 y; 47.8% at 5 yy	NR
Lacaille et al (2017)	• Isolated IT • Combined liver IT • Multivisceral graft	45 60 5	• 59% at 10 y; 54% at 18 y • 48% at 10 y • NR	All treatments combined: 73% at last follow-up
Garcia Aroz et al (2017)	• Isolated IT • Combined liver IT	7 3	• All transplantations combined: 70%	All treatments combined: 100% at last follow-up
Dore et al (2016)	• Isolated IT • Combined liver IT • Multivisceral graft	6 6 18	• 83% at 9 y • 33% at 10 y • 67% at 2.5 y	All treatments combined: 71% in 31 d and 62% at last follow-up
Rutter et al (2016)	• Isolated IT • Multivisceral graft • Modified multivisceral	16 35 9	• 92% at 1 y; 37% at 5 y • 71% at 1 y; 33% at 5 y • 85% at 1 y, 65% at 5y	NR
Lauro et al (2014)	• Isolated IT • Combined liver IT • Multivisceral graft	34 6 6	All transplantations combined: • 77% at 1 y • 58% at 3 y • 53% at 5 y • 37% at 10 y	NR
Varkey et al (2013)	• Isolated IT • Combined liver IT • Multivisceral graft	4 1 15	All transplantations combined: • 78% at 1 year • 50 % at 5 y	NR
Mangus et al (2013)	• Multivisceral graft • Modified multivisceral	84 16	All transplantations combined: • 72% at 1 y • 57% at 5 y	NR

IT: intestinal transplantation; NR: not reported; TPN: total parenteral nutrition.
[a] Living donors

Complications

Several case series have focused on complications after small bowel and multivisceral transplantation. For example, Spence et al (2019) performed a retrospective chart review of intra-abdominal and bloodstream infection in adults undergoing intestinal or multivisceral transplant at a single center in the U.S.[17] A total of 103 adult patients (median age, 44 years) were included who received 106 intestinal or multivisceral transplants between 2003 and 2015. Intra-abdominal infection occurred in 46 (43%) patients, and concurrent bloodstream infection occurred in 6 (13%) patients. The median time to first intra-abdominal infection was 23 days (interquartile range, 10-48). All-cause mortality was not significantly different between patients with versus without intra-abdominal infections (p=0.654).

in 2016, Nagai et al reported on cytomegalovirus (CMV) infection after intestinal or multivisceral transplantation at a single center in the United States.[18] A total of 210 patients had an intestinal transplant, multivisceral transplant, or modified multivisceral transplant between January 2003 and June 2014. Median length of follow-up was 2.1 years. Thirty-four (16%) patients developed CMV infection a median of 347 days after transplantation. Nineteen patients had tissue invasive CMV disease. In a report from another U.S. center, 16 (19%) of 85

patients undergoing intestinal or multivisceral transplantation developed CMV infection a mean of 139 days (range, 14-243 days) postoperatively.[19]

In 2016, Wu et al investigated the incidence and risk factors of acute antibody-mediated rejection (ABMR) among patients undergoing intestinal transplantation (N=175).[20] All patients were 25 years of age. Acute ABMR was diagnosed by clinical evidence; histologic evidence of tissue damage; focal or diffuse linear C4d deposition; and circulating anti-human leukocyte antigen antibodies. Of the 175 intestinal transplants, 58% were liver-free grafts, 36% included a liver graft, and 6.3% were retransplantations. Eighteen cases of acute ABMR were identified-14 (14%) among the patients undergoing first liver-free transplantation, 2 (3%) among patients undergoing liver/small bowel transplantations, and 2 (18%) among the patients undergoing retransplantation. Graft failure occurred in 67% of patients with acute ABMR. The presence of a donor-specific antibody and a liver-free graft were associated with the development of acute ABMR.

In a 2016 series by Cromvik et al, 5 (19%) of 26 patients were diagnosed with graft-versus-host disease (GVHD) after intestinal or multivisceral transplantation.[21] Risk factors for GVHD were: malignancy as a cause of transplantation; neoadjuvant chemotherapy; or brachytherapy before transplantation.

In addition, a 2012 article by Florescu et al retrospectively reported on bloodstream infections among 98 children younger than age 18 years with small bowel/combined organ transplants.[22] Seventy-seven (79%) patients underwent small bowel transplant in combination with a liver, kidney or kidney-pancreas, and 21 had an isolated small bowel transplant. After a median follow-up of 52 months, 58 (59%) patients remained alive. The 1-year survival rate was similar in patients with combined small bowel transplant (75%) and those with isolated small bowel transplant (81%). In the first year after transplantation, 68 patients (69.4%) experienced at least one episode of bloodstream infection. The 1-year survival rate for patients with bloodstream infections was 72% compared to 87% in patients without bloodstream infections (p-value= 0.056 for difference in survival in patients with and without bloodstream infections).

In 2011 Wu et al reported on 241 patients who underwent intestinal transplantation.[23] Of these, 147 (61%) had multivisceral transplants, 65 (27%) had small bowel transplants, and 29 (12%) had small bowel/liver transplants. There were 151 (63%) children and 90 (37%) adults. Twenty-two (9%) patients developed graft-versus-host disease (GVHD). Children younger than 5 years old were more likely to develop this condition; the incidence in this age group was 16 (13.2%) of 121 compared with 2 (6.7%) of 30 in children between 5 and 18 years and 9 (4.4%) of 90 in adults older than 18 years.

HIV-Positive Transplant Recipients

Solid organ transplant for patients who are HIV-positive was historically controversial, due to the long-term prognosis for HIV positivity and the impact of immunosuppression on HIV disease. No studies reporting on outcomes in HIV-positive patients who received small bowel and liver or multivisceral transplants were identified in literature reviews.

Current OPTN policy permits HIV-positive transplant candidates.[24]

The British HIV Association and the British Transplantation Society (2017) updated their guidelines on kidney transplantation in patients with HIV disease.[25]These criteria may be extrapolated to other organs:

- Adherent with treatment, particularly antiretroviral therapy
- CD4 count greater than 100 cells/mL (ideally >200 cells/mL) for at least 3 months
- Undetectable HIV viremia (<50 HIV-1 RNA copies/mL) for at least 6 months
- No opportunistic infections for at least 6 months
- No history of progressive multifocal leukoencephalopathy, chronic intestinal cryptosporidiosis, or lymphoma.

Section Summary: Transplantation of Small Bowel/Liver or Multivisceral Organs
Intestinal transplantation procedures are infrequently performed and only one registry study and relatively small case series, generally single-center, are available. For patients experiencing significant complications from TPN, which can lead to liver failure and repeated infections, this literature has shown a reasonably high post-transplant survival rates in patients who have a high probability of death without treatment. Guidelines and U.S. federal policy no longer view HIV infection as an absolute contraindication for solid organ transplantation.

Modified Multivisceral Transplantation
In 2007, Matsumoto and Fishbein discussed a modified multivisceral technique where the native spleen and pancreas were preserved with venous outflow through a native portocaval shunt, and native pancreatic exocrine drainage was established to the donor jejunum.[26] According to the authors, the risk of transplant pancreatic insufficiency, posttransplant lymphoproliferative disorder, and postsplenectomy sepsis was avoided. This new modification of multivisceral transplantation allows pancreaticosplenic preservation while facilitating stomach replacement for those patients requiring intestinal replacement therapy. It represents another step towards minimizing morbidities associated with these lifesaving transplants.

Cruz et al (2010) reported on a modification of a multivisceral transplant operation where the donor liver was spared, and the native spleen along with pancreaticoduodenal complex was preserved.[27] Thirty-six modified multivisceral grafts that include stomach, duodenum, pancreas, and intestine were given to 30 adults and six children. Leading causes of intestinal failure were pseudo-obstruction and Gardner's syndrome. Native spleen was preserved in 24 (67%) recipients along with pancreaticoduodenal complex in 18 (50%). Immunosuppression was tacrolimus-based, and recipient preconditioning was utilized in 80% of patients. Patient survival was 94% at 1 year and 75% at 5 years with graft survival of 91% and 51%;respectively. With mean follow-up of 51 ± 35 months, full nutritional autonomy was achieved in 89%of current survivors with no single example of disease recurrence. Preservation of native spleen was associated with increased survival and reduced risk of PTLD, life-threatening infections, and GVHD with no significant impact on graft loss due to rejection. Concomitant preservation of pancreaticoduodenal complex eliminated risks of biliary complications and glucose intolerance.

In a retrospective case review, Mangus et al (2013) described multivisceral transplantation including the simultaneous transplantation of multiple abdominal viscera including the stomach, duodenum, pancreas, and small intestine, with (multivisceral transplant, MVT) or without the liver (modified MVT, MMVT).[28] During the study period, 95 patients received 100 transplants including 84 MVT and 16MMVT. There were 19 patients who received a simultaneous kidney graft. There were 24 pediatric and76 adult recipients (range 7 months to 66 years). Indications included intestinal failure alone, intestinal failure with cirrhosis, complete portal mesenteric thrombosis, slow-growing central abdominal tumors, intestinal pseudo obstruction, and frozen abdomen. All patients received antibody-based induction immunosuppression with calcineurin inhibitor-based maintenance immunosuppression. At a

median mortality adjusted follow-up of 25 months, 1- and 3-year patient survival is 72 % and 57 %. There was a learning curve with this complex procedure resulting in a 48 % patient survival during the period from 2004 to 2007, followed by a 70 % patient survival during the period from 2008 to 2010. Post-transplant complications included rejection (50 % MMVT and 17 % MVT), infection (>90 % first year),graft versus host disease (13 %), and post-transplant lymphoproliferative disorder (5 %).

RETRANSPLANTATION OF SMALL BOWEL AND LIVER OR MULTIVISCERAL ORGANS

Clinical Context and Therapy Purpose

The purpose of small bowel and liver retransplant alone or multivisceral retransplant in patients who have a failed small bowel and liver or multivisceral transplant without contraindications for retransplant is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following **PICOs** were used to select literature to inform this review.

Populations

The relevant population of interest is individuals with a failed small bowel and liver or multivisceral transplant without contraindications for retransplant.

Interventions

The therapy being considered is small bowel and liver retransplant alone or multivisceral retransplant.

Comparators

The following practices are currently being used to make decisions about failed small bowel and liver or multivisceral transplant when there are no contraindications for retransplant: medical management and parenteral nutrition.

Outcomes

The general outcomes of interest are OS, morbid events, treatment-related mortality, and treatment-related morbidity.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Within each category of study design, studies with larger sample sizes and longer duration were preferred.
- Studies with duplicative or overlapping populations were excluded.

Case Series

Evidence for the use of retransplantation to treat individuals who have failed intestinal transplantations includes several case series, mostly from single institutions. One case series analyzed records from the United Network for Organ Sharing database.[9] Among the case

series described in Table 3, reasons for retransplantations include: acute rejection, chronic rejection, CMV, liver failure, lymphoproliferative disorder, and graft dysfunction. Survival rates for retransplantations are listed in Table 4.

Table 3. Summary of Key Case Series Characteristics for Retransplants

Author (Year	Location	N	Median Age (Range), y	Interventions		Follow-Up, (Range), mo
				Treatment	**n**	
Ekser et al (2018)	U.S.	18[b]	27.0 (17.4)[a] (0.9 to 57)	• Isolated IT • Modified MVT • Multivisceral graft	1 1 16	NR
Lucaille et al (2017)	France	10	13 (5-16)	• Isolated IT • Combined liver IT	3 7	4
Desai et al (2012)	United States	72 adults 77 children	NR	Adults: • Isolated IT • Combined liver IT Children: • Isolated IT • Combined liver IT	 41 31 28 49	NR
Abu-Elmage et al (2009)	United States	47	NR	• Isolated IT • Combined liver IT • Multivisceral graft	31 7 9	NR
Mazariegos et al (2008)	United States	14	9.4 (3.2-22.7)	• Isolated IT • Combined liver • Multivisceral graft	1 3 10	55.9

IT: intestinal transplantation; NR: not reported
[a] Mean (standard deviation).
[b] Of a cohort of 218 transplant or retransplant procedures.

Table 4. Summary of Key Case Series Results for Retransplantations

Author (Year)	Interventions		Survival	Off TPN
	Treatment	**n**		
Ekser et al (2018)	• Isolated IT • Modified MVT • Multivisceral graft	1 1 16	Graft survival: • 71% at 1 y; 56% at 3 y; 44% at 5 y Patient survival • 71% at 1 y; 47% at 3 y; 37% at 5 y	NR
Lucaille et al (2017)	• Isolated IT • Combined liver IT	3 7	All transplantations combined: 30% at last follow-up	NR
Desai et al (2012)	Adults: • Isolated IT • Combined liver IT Children: • Isolated IT Combined liver IT	 41 31 28 49	Adults: • 80% at 1 y; 47% at 3 y; 29% at 5y • 53% at 1 y; 56% at 3 y; 47% at 5 Y	NR
Abu-Elmage et al (2009)	• Isolated IT • Combined liver IT Multivisceral graft	31 7 9	All transplantations combined: • 69% at 1 y • 47% at 5 y	NR
Mazariegos et al (2008)	• Isolated IT • Combined liver	1 3	All transplantations combined: • 71% at last follow-up	100%

	Multivisceral graft	10		

IT: intestinal transplantation; NR: not reported; TPN: total parenteral nutrition.

Section Summary: Retransplantation of Small Bowel/Liver or Multivisceral Organs
Evidence for retransplantations derives mostly from single-center case series, though 1 series used records from the United Network for Organ Sharing database. Although limited in quantity, the available follow-up data after retransplantation have suggested reasonably high survival rates after small bowel and liver transplants and multivisceral retransplantation in patients who continue to meet criteria for transplantation.

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 registry study and a limited number of case series. Relevant outcomes are overall survival, morbid events, and treatment-related mortality and morbidity. These procedures are infrequently performed and only relatively small case series, generally single-center, are available. Results from the available literature have shown reasonably high postprocedural survival rates. Given exceedingly poor survival rates without transplantation of patients who have exhausted other treatments, evidence of postoperative survival from uncontrolled studies is sufficient to demonstrate that small bowel/liver and multivisceral transplantation provides a survival benefit in appropriately selected patients. Transplantation is contraindicated for patients in whom the procedure is expected to be futile due to comorbid disease or in whom post transplantation 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 intestinal failure and evidence of other multivisceral failure, the evidence includes literature describing a modified multivisceral transplantation procedure, and a retrospective case review. This modified technique represents another step towards minimizing morbidities associated with lifesaving transplants and decreasing risks of biliary complications and glucose intolerance. 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. Relevant outcomes are overall survival, morbid events, and treatment-related mortality and morbidity. Although limited in quantity, the available post retransplantation data has 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 post transplantation 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.

SUPPLEMENTAL INFORMATION

PRACTICE GUIDELINES AND POSITION STATEMENTS

American Gastroenterological Association

In 2003, the American Gastroenterological Association published a position statement on short bowel syndrome and intestinal transplantation.[29]The statement noted that only patients with life-threatening complications due to intestinal failure or long-term total parenteral nutrition have undergone intestinal transplantation. The statement recommended the following Medicare-approved indications, pending availability of additional data:

- Impending liver failure
- Thrombosis of major central venous channels
- Frequent central line associated sepsis
- Frequent severe dehydration.

The AGA published an expert review update in 2022.[29.] The update made the same statements as the 2003 position statement in their best practice advice for referral for intestinal transplantation.

American Society of Transplantation

In 2001, the American Society of Transplantation issued a position paper on indications for pediatric intestinal transplantation.[30] The Society listed the following disorders in children as being potentially treatable by intestinal transplantation: short bowel syndrome, defective intestinal motility, and impaired enterocyte absorptive capacity. Contraindications for intestinal transplant to treat pediatric patients with intestinal failure are similar to those of other solid organ transplants: profound neurologic disabilities, life threatening comorbidities, severe immunologic deficiencies, nonresectable malignancies, autoimmune diseases, and insufficient vascular patency.

Ongoing and Unpublished Clinical Trials

A search of ClinicalTrials.gov did not identify any ongoing or unpublished trials that would likely influence this policy.

Government Regulations
National/Local:

Medicare will cover intestinal transplantation for the purposes of restoring intestinal function in patients with irreversible intestinal failure only when performed for patients who have failed TPN and only when performed in centers that meet approved criteria.[31]The criteria for approval of centers will be based on an annual volume of 10 intestinal transplants per year with a 1-year actuarial survival of 65% (these criteria were reviewed again in 2006 and upheld).

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Heart Transplant
- Heart-Lung Transplant
- Isolated Small Bowel Transplant
- Liver Transplant
- Lung and Lobar Lung Transplant
- Pancreas Transplant

References

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through September 2023, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
7/1/12	4/10/12	5/18/12	The consolidated policy "small bowel of Small Bowel/Liver-Multivisceral Transplants" was split into two separate policies: Small Bowel Transplant- Isolated and this policy, Small Bowel/Liver-Multivisceral Transplant. Updated description, rationale and references to mirror BCBSA policies.
11/1/13	8/22/13	8/27/13	Routine maintenance Added "small bowel/liver transplant or multivisceral retransplant after a failed primary small bowel/liver transplant or multivisceral transplant" to the inclusions. Removed procedure codes 44135-44136.
3/1/15	12/12/14	12/29/14	Routine maintenance. No substantive changes to policy. Statement added that procedure is investigational in all other situations.
7/1/16	4/19/16	4/19/16	Routine maintenance. No change in policy statement
7/1/17	4/18/17	4/18/17	Updated rationale and added references # 2, 6, 7, 9, 14 and 20. Deleted references 1 and 10. Deleted code 47136, added code 47399. No change in policy status.
7/1/18	4/17/18	4/17/18	Updated rationale section, added references # 7-9 and 15. No change in policy status.
7/1/19	4/16/19		Routine policy maintenance. No change in policy status.
7/1/20	4/14/20		Routine policy maintenance. No change in policy status.
7/1/21	4/20/21		Routine policy maintenance. Added reference #9. No change in policy status.
7/1/22	4/19/22		Routine policy maintenance, no change in policy status.
1/1/23	10/18/22		Added modified multivisceral transplant to MPS as established,

			updated rationale section, added references 2 and 26-28. No change in policy status.
1/1/24	10/17/23		Routine policy maintenance, no change in policy status. Vendor managed: N/A (ds)

Next Review Date: 4th Qtr. 2024

Joint BCBSM/BCN Consolidated Medical Policy History (Small Bowel or Small Bowel/Liver or Multivisceral Transplant)

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
6/13/02	6/13/02	6/13/02	Joint medical policy established
11/8/04	11/8/04	12/6/04	Routine maintenance
11/15/05	11/15/05	9/26/05	Routine maintenance
9/1/06	7/10/06	7/6/06	Routine maintenance
9/1/07	7/1/07	8/26/06	Routine maintenance
11/1/08	8/19/08	10/30/08	Routine maintenance

No further review will be done on the consolidated policy; refer to separate policies on

- Small Bowel Transplant-Isolated and
- Small Bowel/Liver and Multivisceral Transplant

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: SMALL BOWEL/LIVER AND MULTIVISCERAL TRANSPLANT

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered; policy guidelines apply Transportation, meals and lodging expenses related to the transplant are not covered unless specifically noted in the member's certificate/rider.
BCNA (Medicare Advantage)	See government section.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service. Transportation, meals and lodging expenses related to the transplant are not covered unless specifically noted in the member's certificate/rider.

Note: All services related to the transplant, except evaluation services, will not be authorized until the transplant is approved.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.