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Small Bowel/Liver and Multi-visceral Transplant

Policy Number: MM.07.025	**Current Effective Date:** November 17, 2023
Lines of Business: HMO; PPO	**Original Effective Date:** May 23, 2001
Place of Service: Inpatient	**Precertification:** Required, refer to Section V

I. Description

Small bowel/liver transplantation is transplantation of an intestinal allograft in combination with a liver allograft, either alone or in combination with 1 or more of the following organs: stomach, duodenum, jejunum, ileum, pancreas, or colon.

Small bowel transplants are typically performed in individuals 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. In some instances, short bowel syndrome is associated with liver failure, often due to the long-term complications of total parenteral nutrition (TPN). These individuals may be candidates for a small bowel/liver transplant or a multi-visceral transplant, which includes the small bowel and liver with 1 or more of the following organs: stomach, duodenum, jejunum, ileum, pancreas, and/or colon. A multi-visceral transplant is indicated when anatomic or other medical problems preclude a small bowel/liver transplant.

II. Policy Criteria

A. A small bowel and liver transplant or multi-visceral transplant is covered (subject to Administrative Guidelines) for pediatric and adult 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 impending end-stage liver failure (refer to Policy Guidelines).

B. A small bowel and liver retransplant or multi-visceral retransplant is covered (subject to Administrative Guidelines) after a failed primary small bowel/liver transplant or multi-visceral transplant.

C. Candidates must meet **BOTH** the following:
   1. Adequate cardiopulmonary status.
   2. Documentation of individual compliance with medical management.

D. HIV-positive individuals who meet **ALL** the following, as stated in the 2001 guidelines of the American Society of Transplantation, could be considered candidates for small bowel and liver or multi-visceral transplantation:
   1. The individual has CD4 count > 200 cells per cubic millimeter for greater than 6 months.
   2. HIV-1 RNA is undetectable.
   3. The individual has been on stable anti-retroviral therapy >3 months.
   4. No other complications from AIDS are present (e.g., opportunistic infection including: aspergillus; tuberculosis; coccidiosis mycosis; resistant fungal infections; Kaposi's sarcoma; other neoplasm).
   5. The individual meets all other criteria for transplantation.

III. Policy Guidelines

A. A small bowel transplant in the setting of progressive liver failure may be considered a technique to avoid end-stage liver failure related to chronic TPN, thus avoiding the necessity of a multi-visceral transplant. Evidence of intolerance of TPN includes but is not limited to:
   1. Multiple and prolonged hospitalizations to treat TPN-related complications.
   2. Development of progressive but reversible liver failure.

B. Potential contraindications to solid organ transplant (subject to the judgement of the transplant center):
   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 the individual's ability to adhere to therapy.

IV. Limitations

A small bowel/liver transplant or multi-visceral transplant is not covered in all other situations because it is not known to improve health outcomes.

V. Administrative Guidelines

A. Precertification is required for a transplant evaluation and for the transplant itself and should be submitted by the proposed treating facility. To precertify, complete HMSA's Precertification Request and mail or fax the form or use iExchange as indicated along with the required documentation.

B. Applicable codes

CPT Code	Description
44120	Enterectomy, resection of small intestine; single resection and anastomosis
44121	; each additional resection and anastomosis
44132	Donor enterectomy (including cold preservation), open; from cadaveric donor
44133	; partial, from living donor
44715	Backbench standard preparation of cadaver or living donor intestine allograft prior to transplantation, including mobilization and fashioning of the superior mesenteric artery and vein
44720	Backbench reconstruction of cadaver or living donor intestine allograft prior to transplantation, venous anastomosis, each
44721	; arterial anastomosis, each
44799	Unlisted procedure, intestine
47133	Donor hepatectomy (including cold preservation), from cadaver donor
47135	Liver allotransplantation, orthotopic, partial or whole, cadaver or living donor, any age
47140	Donor hepatectomy (including cold preservation), from living donor; left lateral segment only (segments II and III)
47141	; total left lobectomy (segments II, III, or IV)
47142	; total right lobectomy (segments V, VI, VII, and VIII)
47143	Backbench standard preparation of cadaver donor whole liver graft prior to allotransplantation, including cholecystectomy, if necessary, and dissection and

	removal of surrounding tissues to prepare the vena cava, portal vein, hepatic artery, and common bile duct for implantation; without trisegment or lobe split
47144	; with trisegment split of whole liver graft into two partial liver grafts (i.e., left lateral segment (segments II and III) and right trisegment (segments I and IV through VIII))
47145	; with lobe split of whole liver graft into two partial liver grafts (i.e., left lobe (segments II, III and IV) and right lobe (segments I and V through VIII))
47146	Backbench reconstruction of cadaver or living donor liver graft prior to allotransplantation; venous anastomosis
47147	; arterial anastomosis, each
47399	Unlisted procedure; liver

HCPCS Code	Description
S2053	Transplantation of small intestine, and liver allografts
S2054	Transplantation of multivisceral organs
S2055	Harvesting of donor multivisceral organs, with preparation and maintenance of allografts; from cadaver donor

ICD-10-CM	Description
K72.00-K72.01	Acute and subacute hepatic failure code range
K72.10-K72.11	Chronic hepatic failure code range
K91.2	Postsurgical malabsorption, not elsewhere classified (includes short bowel syndrome)

ICD-10-PCS	Description
0DY60Z0	Transplantation, stomach, open, allogeneic
0DY80Z0	Transplantation, small intestine, open, allogeneic
0DYE0Z0	Transplantation, large intestine, open, allogeneic
0FY00Z0	Transplantation, liver, open, allogeneic
0FYG0Z0	Transplantation, pancreas, open, allogeneic

VI. Scientific Background

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 multi-visceral transplant, the evidence includes a registry study and a limited number of case series. Relevant outcomes are overall survival (OS), 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 literature 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 post-transplantation care is expected to significantly worsen comorbid conditions. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have a failed small bowel and liver or multi-visceral transplant without contraindications for retransplant who receive a small bowel and liver retransplant alone or multi-visceral retransplant, the evidence includes case series. Relevant outcomes are OS, morbid events, and treatment-related mortality and morbidity. Although limited in quantity, the available post re-

transplantation data have suggested reasonably high survival rates. Given exceedingly poor survival rates without re-transplantation of patients who have exhausted other treatments, evidence of postoperative survival from uncontrolled studies is sufficient to demonstrate that re-transplantation provides a survival benefit in appropriately selected patients. Re-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 an improvement in the net health outcome.

Solid Organ Transplantation

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. 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 Multi-visceral Transplant

In 2022, 42,889 transplants were performed in the United States procured from 36,421 deceased donors and 6,468 living donors. 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 multi-visceral 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

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 multi-visceral 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. A multi-visceral transplant is indicated when anatomic or other medical problems preclude a small bowel/liver transplant. Complications following small bowel/liver and multi-visceral transplants include acute or chronic rejection, donor-specific antibodies, infection, lymphoproliferative disorder, graft-versus-host disease, and renal dysfunction.

Regulatory Status

Small bowel/liver and multi-visceral 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.

Rationale

This evidence review was created in December 1995 and has been updated regularly with searches of the MEDLINE database. The most recent literature update was performed through June 28, 2023.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are the 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 (RCT) 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 and Liver or Multi-visceral Organs

Clinical Context and Therapy Purpose

The purpose of small bowel and liver transplant alone or multi-visceral 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 PICO was used to select literature to inform this review.

Populations

The relevant population of interest are 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, including short- and long-term graft survival and 1- and 5-year OS.

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.

Review of Evidence

Systematic Reviews
A TEC Assessment (1999) focused on multi-visceral transplantation and offered the following conclusions:

"Multi-visceral 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 is associated with poor patient and graft survival. Pediatric and adult patients have a similar 2- and 5-year survival of 33% to 50%. However, without this procedure, it is expected that these patients would face 100% mortality."

Registry Studies and Case Series
The published literature consists of case series, mainly reported by single centers in the U. S. and Europe. Tables 1 and 2 summarize the characteristics and results of the case series, respectively. Many case series have included isolated small bowel transplantations (see evidence review 7.03.04).

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. 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 multi-visceral transplants (see Table 2).

Several investigators have reported higher survival rates in transplants conducted more recently than those conducted earlier. 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 series, 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 Transplantations

Populations, Individuals:	Interventions of interest:	Comparators of interest:	Outcomes
With intestinal failure and evidence of impending end-stage liver failure	• small bowel and liver transplant alone • multivisceral transplant	• medical management • parenteral nutrition	• overall survival • morbid events • treatment-related mortality • treatment-related morbidity
With a failed small bowel and liver or multivisceral transplant without contraindications for retransplant	• small bowel and liver transplant alone • multivisceral transplant	• medical management • parenteral nutrition	• overall survival • morbid events • treatment-related mortality • treatment-related morbidity

Study	Country	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])	725966389	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)	U.S.	10	1.5 (0.7-13)	• Isolated IT • Combined liver IT	• 7 • 3	6/7 alive at ≥10 y
Dore et al (2016)	U.S.	30	0.2 (0.1-18)	• Isolated IT • Combined liver IT • Multivisceral graft	• 6 • 6 • 18	28 (4-175) mo
Rutter et al (2016)	U.K.	60	1.8 (0-8)	• Isolated IT • Combined liver IT • 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 (0.52-13)	• Isolated IT • Combined liver IT • Multivisceral graft	• 4 • 1 • 15	NR
Mangus et al (2013)	U.S.	100	Adults: 48 (NR to 66)	• Multivisceral graft • Modified multivisceral	• 84 • 16	25 mo

			Children: 1 (0.6 to NR)			

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

Table 2. Summary of Key Case Series Results for Transplantations

Study	Interventions		Survival	Off TPN
	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 y	NR
Lacaille et al (2017)	• Isolated IT Combined liver IT Multivisceral graft	60 45 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 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 5 y	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 y • 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 multi-visceral transplantation. For example, Spence et al (2020) performed a retrospective chart review of intra-abdominal and bloodstream infection in adults undergoing intestinal or multi-visceral transplant at a single center in the U.S. A total of 103 adult patients (median age, 44 years) were included who received 106 intestinal or multi-visceral 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 to 48). All-cause mortality was not significantly different between patients with versus without intra-abdominal infections (p=.654).

Nagai et al (2016) reported on cytomegalovirus (CMV) infection after intestinal or multi-visceral transplantation at a single center in the U.S. A total of 210 patients had either an intestinal transplant, multi-visceral transplant, or modified multi-visceral transplant between 2003 and

2014. The median length of follow-up was 2.1 years. Thirty-four (16%) patients developed CMV infection at a median of 347 days after transplantation. Nineteen patients had tissue-invasive CMV disease. CMV infection was significantly associated with rejection (odds ratio, 2.6; p<0.01) and adversely affected patient survival (hazard ratio, 2.7; p<0.001). In a 2016 report from another U.S. center, Timpone et al (2016) reported that 16 (19%) of 85 patients undergoing intestinal or multi-visceral transplantation developed CMV infection a mean of 139 days (range, 14-243) post-operatively.

Wu et al (2016) investigated the incidence and risk factors of acute antibody-mediated rejection (ABMR) among patients undergoing intestinal transplantation (n=175). 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 re-transplantations. Eighteen cases of acute ABMR were identified-14 (14%) among the patients undergoing first liver-free transplantation, 2 (3%) among patients undergoing liver and small bowel transplantations, and 2 (18%) among the patients undergoing re-transplantation. 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 series by Cromvik et al (2016), 5 (19%) of 26 patients were diagnosed with graft-versus-host disease after intestinal or multi-visceral transplantation. Risk factors for graft-versus-host disease were: malignancy as a cause of transplantation; neoadjuvant chemotherapy; or brachytherapy before transplantation.

In a retrospective study, Florescu et al (2012) reported on bloodstream infections among 98 children (>18 years) with small bowel and combined organ transplants. Seventy-seven (79%) underwent small bowel transplant in combination with a liver, kidney, or kidney and pancreas, and 21 had an isolated small bowel transplant. After a median follow-up of 52 months, 58 (59%) patients had survived. 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 (69.4%) patients experienced at least 1 episode of bloodstream infection. The 1-year survival rate for patients with bloodstream infections was 72% compared with 87% in patients without bloodstream infections (p=0.056 for the difference in survival in patients with and without bloodstream infections).

Wu et al (2011) reported on 241 patients who underwent intestinal transplantation. Of these, 147 (61%) had multi-visceral transplants, 65 (27%) had small bowel transplants, and 29 (12%) had small bowel/liver transplants. Recipients included 151 (63%) children and 90 (37%) adults. Twenty-two (9%) patients developed graft-versus-host disease. Children younger than 5 years old were more likely to develop this condition (13.2% [16/121]) than children between 5 and 18 years (6.7% [2/30]) and adults older than 18 years (4.4% [9/90]).

Human Immunodeficiency Virus-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 Organ Procurement Transplantation Network policy permits HIV-positive transplant candidates.

The British HIV Association and the British Transplantation Society (2017) updated their guidelines on kidney transplantation in patients with HIV disease. 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 six 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 1 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 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.

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 PICO was used to select literature to inform this review.

Populations
The relevant population of interest are 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, including short- and long-term graft survival and 1- and 5-year OS.

Study Selection Criteria

Methodologically credible studies were selected using the the principles described in the first indication.

Case Series

Evidence for the use of re-transplantation to treat individuals who have failed intestinal transplantations includes several case series, mostly from single institutions. The case series by Desai et al (2012) analyzed records from the United Network for Organ Sharing database. Among the case series described in Table 3, reasons for re-transplantations included: acute rejection, chronic rejection, CMV, liver failure, lymphoproliferative disorder, and graft dysfunction. Survival rates for re-transplantations are listed in Table 4.

Table 3. Summary of Key Case Series Characteristics for Re-transplantations

Study	Country	N	Median Age (Range), y	Interventions		Follow-Up (Range)
				Treatment	n	
Ekser et al (2018)	U.S.	18b	27.0 (17.4)a (0.9 to 57)	• Isolated IT • Modified MVT • Multivisceral graft	1 1 16	NR
Lacaille et al (2017)	France	10	13 (5-16)	• Isolated IT • Combined liver IT	3 7	4
Desai et al (2012)	U.S.	72 (adults 77 (children)	NR	Adults: • Isolated IT • Combined liver IT Children: • Isolated IT • Combined liver IT	 41 31 28 49	NR
Abu-Elmagd et al (2009)	U.S.	47	NR	• Isolated IT • Combined liver IT • Multivisceral graft	31 7 9	NR
Mazariegos et al (2008)	U.S.	14	94	• Isolated IT • Combined liver IT • Multivisceral graft	1 3 10	55.9

IT: intestinal transplantation; MVT: multivisceral transplantation; NR: not reported.

[a] Mean (standard deviation).

[b] Of a cohort of 218 transplants or retransplant procedures**.**

Table 4. Summary of Key Case Series Results for Re-transplantation

Study	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
Lacaille 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	 41 31	Adults: 80% at 1 y; 47% at 3 y; 29% at 5 y 63% at 1 y; 56% at 3 y; 47% at 5 y	NR

	Children: • Isolated IT • Combined liver IT	28 49	Children: 81% at 1 y; 74% at 3 y; 57% at 5 y 42% at 1 y; 42% at 3 y; 42% at 5 y	
Abu-Elmagd 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 IT • Multivisceral graft	1 3 10	All transplantations combined: 71% at last follow-up	100%

IT: intestinal transplantation; MVT: multi-visceral transplant; NR: not reported; TPN: total parenteral nutrition.

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

VII. Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

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.

American Gastroenterological Association
In 2003, the American Gastroenterological Association published a position statement on short bowel syndrome and intestinal transplantation. 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

American Society of Transplantation
In 2001, the American Society of Transplantation issued a position paper on indications for pediatric intestinal transplantation. 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.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage

Medicare covers intestinal transplantation for the purposes of restoring intestinal function in patients with irreversible intestinal failure only when performed for patients who have failed total parenteral nutrition and only when performed in centers that meet approved criteria. The criteria for approval of centers are based on a "volume of 10 intestinal transplants per year with a 1-year actutimes survival rate of 65 percent."

Ongoing and Unpublished Clinical Trials

A search of ClinicalTrials.gov in July 2022 did not identify any ongoing or unpublished trials that would likely influence this review.

VIII. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii's Patients' Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), or for QUEST members, under Hawaii Administrative Rules (HAR 1700.1-42), generally accepted standards of medical practice and review of medical literature and government approval status. Medicare defines medical necessity as health care services or supplies needed to diagnose or treat an illness, injury, condition, disease, or its symptoms and that meet accepted standards of medicine. This definition applies only to Medicare Advantage (PPO and HMO) plans.

HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA's determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

IX. References

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X. Policy History

Action Date	Action
December 1, 1995	Policy issued by BCBSA
December 1, 1999	Policy revised by BCBSA
March 21, 2001	Policy approved by UMC
March 23, 2001	Policy approved by QMC
May 8, 2001	Policy approved by QIC
September 4, 2001	Policy approved by Medical Directors
October 17, 2001	Policy approved by UMC
November 13, 2001	Policy approved by QIC
November 16, 2001	Policy approved by QMC
August 20, 2002	Policy approved by Medical Directors
September 13, 2002	Policy approved by UMC
November 12, 2002	Policy approved by QIC
September 2, 2003	Policy approved by Medical Directors
September 12, 2003	Policy approved by UMC
November 18, 2003	Policy approved by QIC
September 7, 2004	Policy approved by Medical Directors
October 8, 2004	Policy approved by UMC
November 9, 2004	Policy approved by QIC
September 20, 2005	Policy approved by Medical Directors
October 21, 2005	Policy approved by UMC
November 8, 2005	Policy presented to QIC
December 5, 2006	Policy approved by Medical Directors
December 15, 2006	Policy approved by UMC
September 18, 2007	Policy reviewed by Medical Director Joseph Humphry, M.D.
September 18, 2007	Policy approved by Medical Directors
October 19, 2007	Policy approved by UMC
November 13, 2007	FYI only to QIC
July 1, 2008	Policy reviewed by Medical Director Mark Mugiishi, M.D.
July 1, 2008	Policy approved by Medical Directors
July 18, 2008	Policy approved by UMC

May 19, 2009	Policy reviewed by Medical Director Mark Mugiishi, M.D.
May 19, 2009	Policy approved by Medical Directors
June 26, 2009	Policy approved by UMC
October 5, 2010	Policy reviewed by Medical Director Mark Mugiishi, M.D.
October 5, 2010	Policy approved by Medical Directors
October 22, 2010	Policy approved by UMC
September 13, 2011	Policy reviewed by Medical Director Mark Mugiishi, M.D.
September 20, 2011	Policy approved by Medical Directors
September 23, 2011	Policy approved by UMC
July 24, 2012	Policy reviewed by Medical Director Mark Mugiishi, M.D.
August 7, 2012	Policy approved by Medical Directors
August 24, 2012	Policy approved by UMC
September 3, 2013	Policy reviewed by Medical Director Stephen Lin, M.D.
September 3, 2013	Policy approved by Medical Directors
September 3, 2013	Policy approved by UMC
July 15, 2014	Policy reviewed by Medical Director Mark Mugiishi, M.D.
July 15, 2014	Policy approved by Medical Directors
July 25, 2014	Policy approved by UMC
June 15, 2015	Policy reviewed by Medical Director Mark Mugiishi, M.D.
July 7, 2015	Policy approved by Medical Directors
July 24, 2015	Policy approved by UMC
April 24, 2017	Policy reviewed by Medical Director Andrew Perry, M.D.
May 16, 2017	Policy approved by Medical Directors
May 26, 2017	Policy approved by UMC
October 29, 2019	Policy reviewed by Medical Director Stephen Lin, M.D.
November 5, 2019	Policy approved by Medical Directors
November 15, 2019	Policy approved by UMC
September 29, 2020	Policy reviewed by Medical Director Stephen Lin, M.D.
October 6, 2020	Policy approved by Medical Directors
October 23, 2020	Policy approved by UMC
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October 11, 2022	Policy reviewed by Medical Director Stephen Lin, M.D.
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November 1, 2023	Policy reviewed by Medical Director Stephen Lin, M.D.
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