7.03.05	Small Bowel/Liver and Multivisceral Transplant		
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Policy Statement

Transplants, such as a multivisceral transplant and a small bowel and liver transplant, may be considered **medically necessary** for pediatric and adult patients when **all** of the following criteria are met:

I. Have been managed with long-term total parenteral nutrition
II. Have developed evidence of impending end-stage liver failure
III. Intestinal failure (characterized by loss of absorption and the inability to maintain protein-energy, fluid, electrolyte, or micronutrient balance)

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.

The transplantation of Hepatitis C Virus (HCV)-viremic solid organs (kidney, lung, heart, liver, small bowel, pancreas) to a HCV non-viremic recipient with a plan to use direct-acting antiviral treatment for HCV is considered **investigational**.

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

The American Society of Transplantation Consensus Conference on the use of hepatitis C viremic donors in solid organ transplantation concluded that the transplantation of organs from HCV viremic donors into HCV-negative recipients should be conducted only under monitored IRB-approved protocols and studies. (See Supplemental Information).

General Criteria

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

- 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.

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 an example 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 and would thus avoid the necessity of a multivisceral transplant.

Description

This evidence review addresses transplantation and retransplantation 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.

Related Policies

- Isolated Small Bowel Transplant

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

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 (FDA).

The FDA regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation Title 21, parts 1270 and 1271. Solid organs used for transplantation are subject to these regulations.

Rationale

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 2020, 39,036 transplants were performed in the United States procured from 12,588 deceased donors and 5,729 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

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.[3] 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 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]

Literature Review

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 1 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 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 question addressed in this evidence review is: Does small bowel and liver transplant alone or multivisceral transplant improve the net health outcome in individuals with intestinal failure and evidence of impending end-stage liver failure?

The following PICO was 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, 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 Blue Cross Blue Shield Association Technology Evaluation Center (TEC) Assessment (1999) 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 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."[6.]

Registry Studies and Case Series
The published literature consists of a registry study and case series, mainly reported by single centers in the U.S. and Europe. Tables 1 and 2 summarize the characteristics and results of these publications, respectively. Many case series have included isolated small bowel transplantations (see Blue Shield of California Medical Policy: Isolated Small Bowel Transplant).

Reasons for transplantations were mainly short bowel syndrome. Other reasons included congenital enteropathies and motility disorders. Outcomes most commonly 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 or some 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.[7,8,9,10] 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 immune-suppression 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

Study	Country	N	Median Age (Range), y	Interventions		Follow-Up (Range)
				Treatment	n	
Raghu et al (2019)[10]	International	2080	2.5 (1.1 to 6.3)	• Isolated ITx • Combined liver Itx • Multivisceral graft (including modified [intestine and stomach without liver] and full [intestine, stomach, and liver])	725 966 389	5 y
Lacaille et al (2017)[11]	France	110	5.3 (0.4 to 19)	• Isolated Itx • Combined liver Itx • Multivisceral graft	45 60 5	Of 55 alive: • 17 at <5 y • 17 at 5 to 10 y • 21 at ≥10 y
Garcia Aroz et al (2017)[12],[a]	U.S.	10	1.5 (0.7 to 13)	• Isolated Itx • Combined liver Itx	7 3	6/7 alive at ≥10 y
Dore et al (2016)[13]	U.S.	30	0.2 (0.1 to 18)	• Isolated Itx • Combined liver Itx • Multivisceral graft	6 6 18	28 (4 to 175) mo
Rutter et al (2016)[14]	U.K.	60	1.8 (0 to 8)	• Isolated Itx • Combined liver Itx • Modified multivisceral	16 35 9	21.3 (0 to 95) mo
Lauro et al (2014)[15]	Italy	46	34 (NR)	• Isolated Itx • Combined liver Itx • Multivisceral graft	34 6 6	51.3 mo

Study	Country	N	Median Age (Range), y	Interventions		Follow-Up (Range)
Varkey et al (2013)[16.]	Sweden	20	• Adults: 44 (20 to 67) • Children: 6 (0.5 to 13)	• Isolated Itx • Combined liver Itx • Multivisceral graft	4 1 15	NR
Mangus et al (2013)[7.]	U.S.	100	• Adults: 48 (NR to 66) • Children: 1 (0.6 to NR)	• Multivisceral graft • Modified multivisceral	84 16	25 mo

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

Table 2. Summary of Key Registry Studies and Case Series Results for Transplantations

Study	Interventions		Survival	Off TPN
	Treatment	n		
Raghu et al (2019)[10.]	• Isolated ITx • Combined liver ITx • 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)[11.]	• Isolated ITx • Combined liver ITx • Multivisceral graft	60 45 5	59% at 10 y; 54% at 18 y 48% at 10 y NR	All transplantations combined: 73% at last follow-up
Garcia Aroz et al (2017)[12.,a]	• Isolated ITx • Combined liver ITx	7 3	All transplantations combined: 70%	All transplantations combined: 100% at last follow-up
Dore et al (2016)[13.]	• Isolated ITx • Combined liver ITx • Multivisceral graft	66 18	83% at 9 y 33% at 10 y 67% at 2.5 y	All transplantations combined: 71% in 31 d 62% at last follow-up
Rutter et al (2016)[14.]	• Isolated ITx • 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)[15.]	• Isolated ITx • Combined liver ITx • 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

Study	Interventions		Survival	Off TPN
Varkey et al (2013)[16]	• Isolated ITx • Combined liver ITx • Multivisceral graft	4 1 15	All transplantations combined: 78% at 1 y 50% at 5 y	NR
Mangus et al (2013)[7]	• Multivisceral graft • Modified multivisceral	84 16	All transplantations combined: 72% at 1 y 57% at 5 y	NR

ITx: 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 (2020) 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 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 multivisceral transplantation at a single center in the U.S.[18] A total of 210 patients had either an intestinal transplant, multivisceral transplant, or modified multivisceral 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. Cytomegalovirus infection was significantly associated with rejection (odds ratio, 2.6; p<.01) and adversely affected patient survival (hazard ratio, 2.7; p<.001). In a 2016 report from another U.S. center, Timpone et al (2016) reported that 16 (19%) of 85 patients undergoing intestinal or multivisceral transplantation developed CMV infection a mean of 139 days (range, 14 to 243 days) postoperatively.[19]

Wu et al (2016) 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 and 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 series by Cromvik et al (2016), 5 (19%) of 26 patients were diagnosed with graft-versus-host disease after intestinal or multivisceral transplantation.[21] 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.[22] 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=.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.[23] Of these, 147 (61%) had multivisceral 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.[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 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 posttransplant 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 question addressed in this evidence review is: Does small bowel and liver retransplant alone or multivisceral retransplant improve the net health outcome in individuals with a failed small bowel and liver or multivisceral transplant and no contraindications to retransplant?

The following PICO was 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, 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
Case Series
Evidence for the use of retransplantation 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.[9] Among the case series described in Table 3, reasons for retransplantations included: 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 Retransplantations

Study	Country	N	Median Age (Range), y	Interventions		Follow-Up , mo
				Treatment	n	
Ekser et al (2018)[26]	U.S.	18[b]	27.0 (17.4)[a] (0.9 to 57)	• Isolated ITx • Modified multivisceral transplant • Multivisceral graft	1 1 16	NR
Lacaille et al (2017)[11]	France	10	13 (5 to 16)	• Isolated ltx • Combined liver ltx	3 7	4
Desai et al (2012)[9]	U.S.	72 (adults) 77 (children)	NR	Adults: • Isolated ltx • Combined liver ltx Children: • Isolated ltx • Combined liver ltx	41 31 28 49	NR

Study	Country	N	Median Age (Range), y	Interventions		Follow-Up , mo
Abu-Elmagd et al (2009)[8.]	U.S.	47	NR	• Isolated Itx • Combined liver Itx • Multivisceral graft	31 7 9	NR
Mazariegos et al (2008)[27.]	U.S.	14	9.4 (3.2 to 22.7)	• Isolated Itx • Combined liver Itx • Multivisceral graft	1 3 10	55.9

Itx: intestinal 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 Retransplantations

Study	Interventions		Survival	Off TPN
	Treatment	n		
Ekser et al (2018)[26.]	• Isolated ITx • Modified multivisceral transplant • 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)[11.]	• Isolated ITx • Combined liver ITx	3 7	All transplantations combined: • 30% at last follow-up	NR
Desai et al (2012)[9.]	Adults: • Isolated ITx • Combined liver ITx Children: • Isolated ITx • Combined liver ITx	Adults: 41 31 Children: 28 49	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 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	NR
Abu-Elmagd et al (2009)[8.]	• Isolated ITx • Combined liver ITx • Multivisceral graft	31 7 9	All transplantations combined: • 69% at 1 y • 47% at 5 y	NR
Mazariegos et al (2008)[27.]	• Isolated ITx • Combined liver ITx • Multivisceral graft	1 3 10	All transplantations combined: • 71% at last follow-up	100%

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

Section Summary: Retransplantation of Small Bowel and 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 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 posttransplantation 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 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 OS, 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 an improvement in the net health outcome.

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
The American Society of Transplantation (2017) convened a consensus conference of experts to address issues related to the transplantation of hepatitis C virus (HCV) viremic solid organs into HCV non-viremic recipients.[31] Key findings and recommendations are summarized in Table 5.

Table 5. American Society of Transplantation Consensus Conference - Use of HCV Viremic Donors

	Content Area	Key Point
1	Definition of HCV positive	HCV –viremic reflecting a positive NAT should be adopted
2	Data interpretation	HCV antibody status alone limits interpretation of outcomes of transplantation of HCV "positive" organs
3	Transmission and Treatment	Highest risk for unexpected HCV transmission is associated with organ donation from a person who injected drugs within the eclipse or pre-viremic period
4	OPTN policy	No current policies prevent transplantation of HCV-viremic organs into HCV non-viremic recipients
5	Ethical considerations	Transplantation of HCV-viremic organs into HCV non-viremic recipients should be conducted under site specific IRB approved protocols with multi-step informed consent.

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.[28] The statement noted that only patients with life-threatening complications due to intestinal failure or long-term total parenteral nutrition (TPN) 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.[29] 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 TPN and only when performed in centers that meet approved criteria.[30] 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 2021 did not identify any ongoing or unpublished trials that would likely influence this review.

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Documentation for Clinical Review

Please provide the following documentation:

- Referring physician history and physical
- Gastroenterologist and/or Hepatology consultation report and/or progress notes documenting:
  - Diagnosis (including disease staging) and prognosis
  - Synopsis of alternative treatments performed and results
  - Specific transplant type being requested
- Surgical consultation report and/or progress notes
- Results of completed transplant evaluation including:
  - Clinical history
  - Specific issues identified during the transplant evaluation
  - Consultation reports/letters (when applicable)
  - Correspondence from referring physicians (when applicable)
  - Identification of donor for living liver transplant (when information is available)
- Medical social service/social worker and/or psychiatric (if issues are noted) evaluations including psychosocial assessment or impression of patient's ability to be an adequate candidate for transplant
- Radiology reports including:
  - Abdominal CT, ultrasound, and/or MRI
  - CXR
- GI procedure reports:
  - Colonoscopy if > 50 years of age
  - EGD
- Cardiology procedures and respiratory function reports:
  - EKG
  - Cardiac echocardiogram, stress test, and cardiac catheterization (if indicated)
  - Pulmonary function tests (PFTs)
- Laboratory reports

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	44120	Enterectomy, resection of small intestine; single resection and anastomosis
	44121	Enterectomy, resection of small intestine; each additional resection and anastomosis (List separately in addition to code for primary procedure)
	44132	Donor enterectomy (including cold preservation), open; from cadaver donor
	44133	Donor enterectomy (including cold preservation), open; 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	Backbench reconstruction of cadaver or living donor intestine allograft prior to transplantation; arterial anastomosis, each
	44799	Unlisted procedure, small intestine
	47133	Donor hepatectomy (including cold preservation), from cadaver donor
	47135	Liver allotransplantation, orthotopic, partial or whole, from cadaver or living donor, any age
	47140	Donor hepatectomy (including cold preservation), from living donor; left lateral segment only (segments II and III)
	47141	Donor hepatectomy (including cold preservation), from living donor; total left lobectomy (segments II, III and IV)
	47142	Donor hepatectomy (including cold preservation), from living donor; 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 soft tissues to prepare the vena cava, portal vein, hepatic artery, and common bile duct for implantation; without trisegment or lobe split
	47144	Backbench standard preparation of cadaver donor whole liver graft prior to allotransplantation, including cholecystectomy, if necessary, and dissection and removal of surrounding soft tissues to prepare the vena cava, portal vein, hepatic artery, and common bile duct for implantation; with trisegment split of whole liver graft into 2 partial liver grafts (i.e., left lateral segment [segments II and III] and right trisegment [segments I and IV through VIII])
	47145	Backbench standard preparation of cadaver donor whole liver graft prior to allotransplantation, including cholecystectomy, if necessary,

Type	Code	Description
		and dissection and removal of surrounding soft tissues to prepare the vena cava, portal vein, hepatic artery, and common bile duct for implantation; with lobe split of whole liver graft into 2 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, each
	47147	Backbench reconstruction of cadaver or living donor liver graft prior to allotransplantation; arterial anastomosis, each
	47399	Unlisted procedure, liver
HCPCS	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

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
11/26/2014	Policy title change from Small Bowel Transplantation Policy revision with position change
01/01/2016	Coding update
02/01/2017	Policy revision without position change
10/01/2017	Policy revision without position change
10/01/2018	Policy revision without position change
10/01/2019	Policy revision without position change
10/01/2020	Annual review. No change to policy statement. Literature review updated.
10/01/2021	Annual review. No change to policy statement. Literature review updated.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT (No changes)	
BEFORE	**AFTER**
Small Bowel/Liver and Multivisceral Transplant 7.03.05 **Policy Statement:** Transplants, such as a multivisceral transplant and a small bowel and liver transplant, may be considered **medically necessary** for pediatric and adult patients when **all** of the following criteria are met: I. Have been managed with long-term total parenteral nutrition II. Have developed evidence of impending end-stage liver failure III. Intestinal failure (characterized by loss of absorption and the inability to maintain protein-energy, fluid, electrolyte, or micronutrient balance) 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. The transplantation of Hepatitis C Virus (HCV)-viremic solid organs (kidney, lung, heart, liver, small bowel, pancreas) to a HCV non-viremic recipient with a plan to use direct-acting antiviral treatment for HCV is considered **investigational**.	**Small Bowel/Liver and Multivisceral Transplant 7.03.05** **Policy Statement:** Transplants, such as a multivisceral transplant and a small bowel and liver transplant, may be considered **medically necessary** for pediatric and adult patients when **all** of the following criteria are met: I. Have been managed with long-term total parenteral nutrition II. Have developed evidence of impending end-stage liver failure III. Intestinal failure (characterized by loss of absorption and the inability to maintain protein-energy, fluid, electrolyte, or micronutrient balance) 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. The transplantation of Hepatitis C Virus (HCV)-viremic solid organs (kidney, lung, heart, liver, small bowel, pancreas) to a HCV non-viremic recipient with a plan to use direct-acting antiviral treatment for HCV is considered **investigational**.