7.03.04	Isolated Small Bowel Transplant		
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Section:	11.0 Transplant	**Page:**	Page 1 of 17

Policy Statement

A small bowel transplant using cadaveric intestine may be considered **medically necessary** in adult and pediatric patients when **all** of the following criteria have been met:

I. Intestinal failure (characterized by loss of absorption and the inability to maintain protein-energy, fluid, electrolyte, or micronutrient balance),
II. Have established long-term dependence on total parenteral nutrition
III. Developing or have developed severe complications due to total parenteral nutrition (TPN)

A small bowel transplant using a living donor may be considered **medically necessary** only when a cadaveric intestine is not available for transplantation in a patient who meets the criteria noted above for a cadaveric intestinal transplant.

A small bowel retransplant may be considered **medically necessary** after a failed primary small bowel transplant.

A small bowel transplant using living donors is considered **not medically necessary** in all other situations.

A small bowel transplant is considered **investigational** for adult and pediatric patients with intestinal failure who can tolerate total parenteral nutrition (TPN).

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 subject to the judgment of the transplant center include the following:

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

Small Bowel-Specific Criteria
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 1 cause of intestinal failure.

Patients who are developing or have developed severe complications due to total parenteral nutrition (TPN) include, but are not limited to, the following: multiple and prolonged hospitalizations to treat TPN-related complications (especially repeated episodes of catheter-related sepsis) or the development of progressive 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. In those receiving TPN, liver disease with jaundice (total bilirubin greater than 3 mg/dL) is often associated with the development of irreversible, progressive liver disease. The inability to maintain venous access is another reason to consider small bowel transplant in those who are dependent on TPN.

Description

A small bowel transplant may be performed as an isolated procedure or in conjunction with other visceral organs, including the liver, duodenum, jejunum, ileum, pancreas, or colon. Isolated small bowel transplant is commonly performed in patients with short bowel syndrome. Small bowel/liver transplants and multivisceral transplants are considered in Blue Shield of California Medical Policy: Small Bowel/Liver and Multivisceral Transplant.

Related Policies

- Small Bowel/Liver and Multivisceral 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

Solid organ transplants are a surgical procedure 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 the Organ Procurement and Transplantation Network (OPTN) and United Network of Organ Sharing (UNOS).

Short Bowel Syndrome

Short bowel syndrome is a condition in which the absorbing surface of the small intestine is inadequate due to extensive disease or surgical removal of a large portion of the small intestine. The spectrum of clinical disease is widely variable from only single micronutrient malabsorption to complete intestinal failure, defined as the reduction of gut function below the minimum necessary for the absorption of macronutrients and/or water and electrolytes.[2] In adults, etiologies of short bowel syndrome include ischemia, trauma, volvulus, and tumors. In children, gastroschisis, volvulus, necrotizing enterocolitis, and congenital atresia are predominant causes. Although the actual prevalence of short bowel syndrome is not clear primarily due to under-reporting and a lack of reliable patient databases, its prevalence is estimated to be 30 cases per million in the U.S.[2]

Treatment

The small intestine, particularly the ileum, can adapt to some functions of the diseased or removed portion over a period of 1 to 2 years. Prognosis for recovery depends on the degree and location of small intestine damage. Therapy focuses on achieving adequate macro- and micronutrient uptake in the remaining small bowel. Pharmacologic agents have been studied to increase villous proliferation and slow transit times, and surgical techniques have been advocated to optimize remaining small bowel.

However, some patients with short bowel syndrome are unable to obtain adequate nutrition from enteral feeding and become chronically dependent on total parenteral nutrition (TPN). For patients with short bowel syndrome, the rate of parenteral nutrition dependency at 1, 2, and 5 years has been reported to be 74%, 64%, and 48%, respectively.[2] Patients with complications from TPN may be considered candidates for a small bowel transplant. Complications include catheter-related mechanical problems, infections, hepatobiliary disease, and metabolic bone disease. While cadaveric intestinal transplant is the most commonly performed transplant, there has been a recent interest in using living donors.

Intestinal transplants (including multivisceral and bowel/liver) represent a small minority of all solid organ transplants. In 2019 , 81 intestinal transplants were performed in the U.S. (approximately 50% of which were intestine-liver transplants).[3] Overall, both the number of new patients added to the intestinal transplant waiting list (n=103) and the number of intestinal transplants performed declined to their lowest levels in 2019.

Literature Review

Evidence reviews assess the clinical evidence to determine whether the use of 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 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 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.

Small Bowel Transplantation

Clinical Context and Therapy Purpose

The purpose of a small bowel transplant in patients who have an intestinal failure is to provide a treatment option that is an alternative to or an improvement on existing therapies. Parenteral nutrition has been a mainstay of therapy for patients with intestinal failure for decades.[4] Medical advances have resulted in improved survival in parenteral nutrition-dependent patients, primarily through an increased likelihood of weaning (i.e., achieving enteral autonomy) and reduced rates and progression of intestinal failure-associated liver disease and other life-threatening complications of prolonged parenteral nutrition administration.

The question addressed in this evidence review is: Does a small bowel transplant improve the net health outcome in individuals with intestinal failure?

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with intestinal failure.

Interventions

The therapy being considered is a small bowel transplant.

Comparators

The following practices are currently being used to make decisions about intestinal failure: medical management and parenteral nutrition.

Outcomes

The general outcomes of interest are overall survival (OS) and treatment-related adverse events (e.g., immunosuppression, graft failure, surgical complications, infections). See the Adverse Events section for a detailed discussion of potential negative outcomes. Short-term follow-up ranges from immediately postsurgery to 30 days posttransplantation; lifelong follow-up (out to 10 years or more given current survival data) is necessary due to ongoing immunosuppressive drugs and risk of graft failure.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
d. Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

This evidence review has been informed by 2 Blue Cross Blue Shield Association Technology Evaluation Center (TEC) Assessments conducted in the 1990s. The first TEC Assessment (1995) concluded that, in children, small bowel transplant was associated with improved survival rates compared with total parenteral nutrition (TPN) because the associated adverse events for small bowel transplant were offset by severe TPN-related complications.[5] The second TEC Assessment (1999) reevaluated the data on adults and concluded that, because it is not possible to predict which patients would survive longer on TPN versus small bowel transplant, transplantation may be considered a reasonable option in select adults.[6]

Case Series

The majority of the published literature consists of case series, mainly reported by single centers in the U.S., Japan, and Europe. Tables 1 and 2 summarize the characteristics and results of these case series, respectively. Many case series have included small bowel/liver transplantations and multivisceral transplantations (which are the focus of Blue Shield of California Medical Policy: Small Bowel/Liver and Multivisceral Transplant).

The main reason for transplantation was short bowel syndrome. Other reasons included congenital enteropathies and motility disorders. The most commonly reported outcomes were survival rates and weaning off TPN. Several studies have presented survival rates by type of transplantation, while others have combined multiple types of transplants when reporting survival rates. When rates were reported by type of transplant, isolated transplantations had higher survival rates than multivisceral transplants (Table 2).

Several investigators have reported higher survival rates in transplantations conducted more recently than those conducted earlier.[7,8] 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.

Sudan (2010) published a review of the literature on long-term outcomes after intestinal transplantation.[9] Sudan noted that intestinal transplantation had become standard therapy for patients with life-threatening complications from parenteral nutrition therapy. Data from current single center series have indicated 1-year patient survival rates between 78% and 85% and 5-year or more survival rates between 56% and 61%. Concerning pediatric intestinal transplant patients, most achieve normal growth velocity at 2 years posttransplant. However, oral aversion is common; tube feedings are necessary for 45% of children. Sudan also reported on parental surveys of quality of life for pediatric transplant patients in which intestinal transplant patients appear to have modestly improved quality of life compared with those remaining on TPN and slightly worse than matched school-age controls without intestinal disease.

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 adverse events follows the evidence tables.

Table 1. Summary of Key Case Series Characteristics for Transplantations

Study	Location	N	Median Age (Range), y	Interventions		Follow-Up (Range), mo
				Treatment	n	
Lacaille et al (2017)[10]	France	110	5.3 (0.4 to 19)	• Isolated IT • Combined liver IT • Multivisceral graft	60 45 5	Of 55 alive: • 17 at <5 y • 17 at 5 to 10 y • 21 at ≥10 y
Garcia Aroz et al (2017)[11]	U.S.	10	1.5 (0.7 to 13)	• Isolated IT • Combined liver IT	7 3	6/7 alive at follow-up ≥10 y

Study	Location	N	Median Age (Range), y	Interventions		Follow-Up (Range), mo
Dore et al (2016)[12,]	U.S.	30	0.2 (0.1 to 18)	• Isolated IT • Combined liver IT • Multivisceral graft	6 6 18	28 (4 to 175)
Rutter et al (2016)[13,]	U.K.	60	1.8 (0 to 8)	• Isolated IT • Multivisceral graft • Modified multivisceral	16 35 9	21.3 (0 to 95)
Lauro et al (2014)[14,]	Italy	46	34 (NR)	• Isolated IT • Combined liver IT • Multivisceral graft	34 6 6	51.3
Ueno et al (2014) [7,]	Japan	24	0 to 2 y: 6[c] • 3 to 6 y: 6 • 7 to 18 y: 8 • ≥19 y: 4	• Isolated IT • Combined liver IT	23 1	NR
Benedetti et al (2006)[8,,a]	U.S.	11	27 (1.5 to 50)	• Isolated IT	11	NR

IT: intestinal transplantation; NR: not reported.
[a] All living donors.
[b] Twelve living donors and 12 cadaveric donors.
[c] Reported as age range and n.

Table 2. Summary of Key Case Series Results for Transplantations

Study	Interventions		Survival		Off TPN	
	Treatment	n	Years	%	Measure	%
Lacaille et al (2017)[10,]	• Isolated IT • Combined liver • Multivisceral graft	60 45 5	OS at 10 Patient survival for liver-containing grafts at 10 and 18 Patient survival for isolated IT at 10 and 18	52; 48; 45 59; 56	All combined at last FU	73
Garcia Aroz et al (2017)[11,,a]	• Isolated IT • Combined liver IT	7 3	All combined:	70	All combined at last FU	100
Dore et al (2016)[12,]	• Isolated IT • Combined liver IT • Multivisceral graft	6 6 18	9 10 2.5	83 33 67	All combined: • in 31 days • at last FU	 71 62
Rutter et al (2016)[13,]	• Isolated IT • Multivisceral graft • Modified multivisceral	16 35 9	1 5	92; 71; 85 83; 33; 65		NR
Lauro et al (2014)[14,]	• Isolated IT • Combined liver IT • Multivisceral graft	34 6 6	All combined: 1 3 5 10	 77 58 53 37		NR
Ueno et al (2014) [7,]	• Isolated IT • Combined liver IT	23 1	All combined: 1 5	 86 68		80
Benedetti et al (2006)[8,,a]	• Isolated IT	11	1 3	82 82		100

FU: follow-up; IT: intestinal transplantation; NR: not reported; OS: overall survival; TPN: total parenteral nutrition.

[a] All living donors.
[b] Twelve living donors and 12 cadaveric donors.

Adverse Events

Systematic Reviews

One issue discussed in intestinal transplantation literature is an earlier referral to avoid combined liver and intestine transplantation.[15] It has been suggested that removing the restriction on intestinal transplantation to patients who have severe complications from TPN and recommending earlier transplantation may improve survival. However, in a review of the status of intestinal transplantation, Vianna et al (2008) identified no randomized trials that compared intestinal transplantation with long-term TPN; therefore, optimal timing for earlier transplantation has not been established.[16]

Case Series

Wu et al (2016) investigated the incidence and risk factors of acute antibody-mediated rejection (ABMR) among patients undergoing intestinal transplantation (N=175).[17] The mean age of enrolled patients was 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 small intestine 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.

Florescu et al (2012) have published several retrospective reviews of complications in a cohort of 98 pediatric patients. Twenty-one (21.4%) of these children had an isolated small bowel transplant; the remainder had combined transplants. Their 2012 study reported that 68 (69%) of the 98 patients developed at least 1 episode of bloodstream infection.[18] Among patients with an isolated small bowel transplant, the median time to infection for those who developed 1 was 4.5 months (95% CI, 2.4 to 6.7 months). Also in 2012, these researchers reported that 7 (7%) of 98 patients developed cytomegalovirus disease; only 1 had an isolated small bowel transplant.[19] Florescu et al (2010) previously reported that, in 25 (25.5%) of 98 cases reviewed who developed at least 1 episode of fungal infection, *Candida* infection was most common.[20] Mortality rates did not differ significantly between patients who did (32.3%) and did not develop a fungal infection (29.8%; p=.46).

Other series have reported on renal failure after intestinal transplantation. For example, Calvo Pulido et al (2014) reported on 21 adults who underwent intestinal transplantation; 17 were isolated small bowel transplants.[21] Thirteen (62%) patients experienced renal failure; the etiology included high ileostomy output, immunosuppression, and medical treatment. Boyer et al (2013) reported that 7 of 12 children who had an isolated small bowel transplant developed renal function complications at some point after surgery.[22] Before treatment, all patients had normal renal functioning.

Living Donor Transplants

Cadaveric intestines are most commonly used, but recently there has been an interest in using a portion of intestine harvested from a living, related donor. Potential advantages of a living donor include the ability to plan the transplantation electively and better antigen matching, leading to improved management of rejection. Case reports from the 1990s have reported on 1 or 2 patients with different lengths of the ileum or jejunum.[23,24,25,26] While there appear to be few complications to the donors, of the 6 cases reported, 5 recipients remain on TPN for at least part of their caloric intake. One patient was weaned off TPN.

Tables 1 and 2 provide details on case series that used living donors (Garcia Aroz et al [2017],[11] Ueno et al [2014],[7] Benedetti et al [2006][8]). In general, survival rates of recipients with living donors are comparable to rates for recipients of cadaveric donations. Living related donors were reported to have an uneventful recovery. Weight loss and diarrhea were reported among donors, but recovery was without complications.

Human Immunodeficiency Virus-Positive Transplant Recipients
The 2013 HIV Organ Policy Equity Act in the U.S. permitted scientists to carry out research into organ donations from a person with HIV to another HIV-infected person.[27] In 2015, the Organ Procurement and Transplant Network (OPTN) updated its policies to be consistent with the HIV Organ Policy Equity Act.[28] The OPTN and United Network for Organ Sharing (UNOS) policies specify that organs from HIV-positive patients be used only for HIV-positive transplant recipients.

Current OPTN policy permits HIV-positive transplant candidates.[29]

The British HIV Association and the British Transplantation Society (2017) updated their guidelines on kidney and pancreas transplantation in patients with HIV disease.[30] These criteria may be extrapolated to other organs:

- Adherent with treatment, particularly antiretroviral therapy
- Cluster of differentiation 4 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: Small Bowel Transplantation
Small bowel transplant is infrequently performed, and only relatively small case series, generally single center, are available. Risks after small bowel transplant are high, particularly related to infection, but may be balanced against the need to avoid the long-term complications of TPN dependence. In addition, early small bowel transplant may obviate the need for a later combined liver/small bowel transplant. Guidelines and U.S. federal policy no longer view HIV infection as an absolute contraindication for solid organ transplantation.

Small Bowel Retransplantation
Clinical Context and Therapy Purpose
The purpose of small bowel retransplants in patients who have failed small bowel transplant and do not have contraindication(s) 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 retransplant improve the net health outcome in individuals whose small bowel transplant has failed?

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is individuals who have failed small bowel transplant and do not have contraindication(s) for retransplant.

Interventions
The therapy being considered is a small bowel retransplant.

Comparators
The following practices are currently being used to make decisions about the intestinal failure of an initial small bowel transplant: medical management and parenteral nutrition.

The general outcomes of interest are OS and treatment-related adverse events (e.g., immunosuppression, graft failure, surgical complications, infections). See the Adverse Events section for initial transplants for a detailed discussion of potential negative outcomes. Short-term follow-up ranges from immediately postsurgery to 30 days posttransplantation; lifelong follow-up (out to 10 years or more given current survival data) is necessary due to ongoing immunosuppressive drugs and risk of graft failure.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
d. Studies with duplicative or overlapping populations were excluded.

Case Series

A few case series from single institutions and a single analysis of data from the UNOS database have provided evidence on the use of retransplantation in patients who failed primary small bowel transplant. Case series characteristics and results are detailed in Tables 3 and 4, respectively.

Desai et al (2012) have published the most comprehensive reporting of outcomes after repeat small bowel transplant in the U.S.[31] The authors evaluated data for patients in the UNOS database who underwent small bowel transplants in the U.S. between 1987 and 2009.

Table 3. Summary of Key Case Series Characteristics for Retransplantations

Study	Location	N	Median Age (Range), y	Interventions		Follow-Up (Range), mo
				Treatment	n	
Lacaille et al (2017)[10]	France	10	13 (5 to 16)	• Isolated IT • Combined liver IT	3 7	4
Desai et al(2012)[31]	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)[32]	U.S.	47	NR	• Isolated IT • Combined liver IT • Multivisceral graft	31 7 9	NR

IT: intestinal transplantation; NR: not reported.

Table 4. Summary of Key Case Series Results for Retransplantations

Study	Interventions		Survival		Off TPN
	Treatment	n	Years	%	
Lacaille et al (2017)[10]	• Isolated IT • Combined liver IT	3 7	All combined at last follow-up:	30	NR
Desai et al (2012)[31]	Adults: • Isolated IT • Combined liver IT Children:	 41 31	Adults: 1/3/5 (isolated IT); 1/3/5 (Combined liver IT) Children:	 80/47/29; 63/56/47	NR

Study	Interventions		Survival		Off TPN
	• Isolated IT	28	1/3/5 (isolated IT);	81/74/57;	
	• Combined liver IT	49	1/3/5 (Combined liver IT)	42/42/42	
Abu-Elmagd et al (2009)[32,]	• Isolated IT	31	All combined:		NR
	• Combined liver IT	7	1	69	
	• Multivisceral graft	9	5	47	

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

Section Summary: Small Bowel Retransplantation
Data from a small number of patients undergoing retransplantation are available. Although limited in quantity, the available data have suggested reasonably high survival rates after small bowel retransplantation in patients who continue to meet the criteria for transplantation.

Summary of Evidence
For individuals who have intestinal failure who receive a small bowel transplant, the evidence includes case series. Relevant outcomes are OS, morbid events, and treatment-related mortality and morbidity. Small bowel transplant is infrequently performed, and only relatively small case series, generally single-center, are available. Risks after small bowel transplant are high, particularly related to infection, but may be balanced against the need to avoid the long-term complications of TPN dependence. In addition, early small bowel transplant may obviate the need for a later combined liver/small bowel transplant. Transplantation is contraindicated in patients in whom the procedure is expected to be futile due to comorbid disease or in whom posttransplantation care is expected to worsen comorbid conditions significantly. Guidelines and U.S. federal policy no longer view HIV infection as an absolute contraindication for solid organ transplantation. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have failed small bowel transplant without contraindication(s) for retransplant who receive a small bowel retransplant, the evidence includes case series. Relevant outcomes are OS, morbid events, and treatment-related mortality and morbidity. Data from a small number of patients undergoing retransplantation are available. Although limited in quantity, the available data have suggested a reasonably high survival rate after small bowel retransplantation in patients who continue to meet the criteria for transplantation. 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.

Clinical Input From Physician Specialty Societies and Academic Medical Centers
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests from Blue Cross Blue Shield Association, input was received from 2 physician specialty societies and 2 academic medical centers in 2009. The consensus of those providing input was that small bowel transplant should be performed in patients who are developing severe total parenteral nutrition (TPN)-related complications and that small bowel transplant from living donors may be considered when cadaveric intestinal transplants are not available.

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.[36] 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 produced a medical position statement on short bowel syndrome and intestinal transplantation.[33.] It recommended dietary, medical, and surgical solutions. Indications for intestinal transplantation mirrored those of the Centers for Medicare & Medicaid Services. The guidelines acknowledged the limitations of a transplant for these patients. The statement recommended the following Medicare-approved indications, pending availability of additional data:

- "Impending or overt liver failure...
- Thrombosis of major central venous channels...
- Frequent central line-related 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.[34.] The Society listed the following disorders in children as 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

The Centers for Medicare & Medicaid have a national coverage determination on intestinal and multivisceral transplantation. The determination covers these types of transplants only when performed for patients who have failed TPN and only when performed in centers that meet approval criteria.

"1. Failed TPN

The TPN delivers nutrients intravenously, avoiding the need for absorption through the small bowel. TPN failure includes the following:

- Impending or overt liver failure due to TPN induced liver injury.
- Thrombosis of the major central venous channels; jugular, subclavian, and femoral veins.
- Frequent line infection and sepsis.
- Frequent episodes of severe dehydration despite intravenous fluid supplement in addition to TPN.

2. Approved Transplant Facilities

The criteria for approval of centers will be based on a volume of 10 intestinal transplants per year with a 1-year actutimes survival of 65 percent using the Kaplan-Meier technique."[35.]

Ongoing and Unpublished Clinical Trials
A search of ClinicalTrials.gov in June 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)
- 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®	44132	Donor enterectomy (including cold preservation), open; from cadaver donor
	44133	Donor enterectomy (including cold preservation), open; partial, from living donor
	44135	Intestinal allotransplantation; from cadaver donor
	44136	Intestinal allotransplantation; 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
HCPCS	None	

Policy History

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

Effective Date	Action
06/09/1993	New Policy Adoption
02/28/2002	Policy Revision
04/02/2010	Policy title change from Small Bowel Transplantation with or without Liver Transplantation Policy revision with position change
01/03/2011	Policy revision without position change
11/26/2014	Policy title change from Small Bowel Transplantation Policy revision with position change
01/01/2017	Policy revision without position change
02/01/2017	Policy revision without position change
10/01/2017	Policy revision without position change
10/01/2018	Policy revision without position change
11/01/2019	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**
Isolated Small Bowel Transplant 7.03.04 **Policy Statement:** A small bowel transplant using cadaveric intestine may be considered **medically necessary** in adult and pediatric patients when **all** of the following criteria have been met: I. Intestinal failure (characterized by loss of absorption and the inability to maintain protein-energy, fluid, electrolyte, or micronutrient balance) II. Have established long-term dependence on total parenteral nutrition III. Developing or have developed severe complications due to total parenteral nutrition (TPN) A small bowel transplant using a living donor may be considered **medically necessary** only when a cadaveric intestine is not available for transplantation in a patient who meets the criteria noted above for a cadaveric intestinal transplant. A small bowel retransplant may be considered **medically necessary** after a failed primary small bowel transplant. A small bowel transplant using living donors is considered **not medically necessary** in all other situations. A small bowel transplant is considered **investigational** for adult and pediatric patients with intestinal failure who can tolerate total parenteral nutrition (TPN). 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.**	**Isolated Small Bowel Transplant 7.03.04** **Policy Statement:** A small bowel transplant using cadaveric intestine may be considered **medically necessary** in adult and pediatric patients when **all** of the following criteria have been met: I. Intestinal failure (characterized by loss of absorption and the inability to maintain protein-energy, fluid, electrolyte, or micronutrient balance), II. Have established long-term dependence on total parenteral nutrition III. Developing or have developed severe complications due to total parenteral nutrition (TPN) A small bowel transplant using a living donor may be considered **medically necessary** only when a cadaveric intestine is not available for transplantation in a patient who meets the criteria noted above for a cadaveric intestinal transplant. A small bowel retransplant may be considered **medically necessary** after a failed primary small bowel transplant. A small bowel transplant using living donors is considered **not medically necessary** in all other situations. A small bowel transplant is considered **investigational** for adult and pediatric patients with intestinal failure who can tolerate total parenteral nutrition (TPN). 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.**