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# Medical Policy

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## Topic: Small Bowel/Liver and Multivisceral Transplant

**Professional**
Original Effective Date: January 11, 2005
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| Populations | Interventions | Comparators | Outcomes |
|---|---|---|---|
| Individuals:<br>• With intestinal failure and | Interventions of interest are: | Comparators of interest are:<br>• Medical management<br>• Parenteral nutrition | Relevant outcomes include:<br>• Overall survival<br>• Morbid events |

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

## DESCRIPTION

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

### Objective

The objective of this evidence review is to determine whether a small bowel and liver transplant, or a multivisceral transplant (or retransplant), improves the net health outcomes in patients with intestinal failure and impending liver failure.

### Background

### SHORT BOWEL SYNDROME

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

### Treatment

A small bowel/liver transplant or a multivisceral transplant includes the small bowel and liver with one or more of the following organs: stomach, duodenum, jejunum, ileum, pancreas, and/or colon. The type of transplantation depends on the underlying etiology of intestinal failure, quality of native organs, presence or severity of liver disease, and history of prior abdominal surgeries.[1] A multivisceral transplant is indicated when anatomic or other medical problems preclude a small bowel/liver transplant.

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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.[2]

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

The U.S. Food and Drug Administration regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation title 21, parts 1270 and 1271. Pancreas transplants are included in these regulations.

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## POLICY

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

B. 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.

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

## Policy Guidelines

General Criteria

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

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

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3. Candidates should meet the following criteria:
   a. Adequate cardiopulmonary status
   b. 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.

## RATIONALE

This evidence review has been updated with searches of the MEDLINE database. The most recent literature update was conducted through June 7, 2018.

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

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

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**TRANSPLANTATION OF SMALL BOWEL AND LIVER OR MULTIVISCERAL ORGANS**

**Clinical Context and Test 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 PICOTS were used to select literature to inform this review.

*Patients*

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.

*Timing*

Periprocedural complications, short- and long-term graft survival, and 1- and 5-year OS are of interest.

*Setting*

Transplantation of small bowel, liver, or multivisceral transplantation takes place in a tertiary hospital setting.

**Systematic Reviews**

A TEC Assessment (1999) focused on multivisceral transplantation and offered the following conclusions:

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> "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."[3]

**Case Series**

The published literature consists of case series, mainly reported by single centers in the United States 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 (TPN). Several studies have presented survival rates by type of transplantation, while others have combined all types of transplants when reporting survival rates. When rates were reported by type of transplant, isolated transplantations had higher survival rates than multivisceral transplants (see Table 2).

Several investigators have reported higher survival rates in transplants conducted more recently than those conducted earlier.[4-6] 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 Case Series Characteristics for Transplantations**

| Study | Country | N | Median Age (Range), y | Interventions | | Follow-Up (Range) |
|---|---|---|---|---|---|---|
| | | | | Treatment | n | |
| Lacaille et al (2017)[7] | France | 110 | 5.3 (0.4-19) | • Isolated IT<br>• Combined liver IT<br>• Multivisceral graft | 45<br>60<br>5 | Of 55 alive:<br>• 17 at <5 y<br>• 17 at 5-10 y<br>• 21 at ≥10 y |

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| Study | Country | N | Median Age (Range), y | Interventions | | Follow-Up (Range) |
|---|---|---|---|---|---|---|
| Garcia Aroz et al (2017)[8,a] | U.S. | 10 | 1.5 (0.7-13) | • Isolated IT<br>• Combined liver IT | 7<br>3 | 6/7 alive at ≥10 y |
| Dore et al (2016)[9] | U.S. | 30 | 0.2 (0.1-18) | • Isolated IT<br>• Combined liver IT<br>• Multivisceral graft | 6<br>6<br>18 | 28 (4-175) mo |
| Rutter et al (2016)[10] | U.K. | 60 | 1.8 (0-8) | • Isolated IT<br>• Multivisceral graft<br>• Modified multivisceral | 16<br>35<br>9 | 21.3 (0-95) mo |
| Lauro et al (2014)[11] | Italy | 46 | 34 (NR) | • Isolated IT<br>• Combined liver IT<br>• Multivisceral graft | 34<br>6<br>6 | 51.3 mo |
| Varkey et al (2013)[12] | Sweden | 20 | • Adults: 44 (20-67)<br>• Children: 6 (0.5-13) | • Isolated IT<br>• Combined liver IT<br>• Multivisceral graft | 4<br>1<br>15 | NR |
| Mangus et al (2013)[4] | U.S. | 100 | • Adults: 48 (NR to 66)<br>• Children: 1 (0.6 to NR) | • Multivisceral graft<br>• Modified multivisceral | 84<br>16 | 25 mo |

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 | | |
| Lacaille et al (2017)[7] | • Isolated IT<br>• Combined liver IT<br>• Multivisceral graft | 60<br>45<br>5 | • 59% at 10 y; 54% at 18 y<br>• 48% at 10 y<br>• NR | All treatments combined:<br>• 73% at last follow-up |
| Garcia Aroz et al (2017)[8,a] | • Isolated IT<br>• Combined liver IT | 7<br>3 | All transplantations combined:<br>• 70% | All treatments combined:<br>• 100% at last follow-up |
| Dore et al (2016)[9] | • Isolated IT<br>• Combined liver IT<br>• Multivisceral graft | 6<br>6<br>18 | • 83% at 9 y<br>• 33% at 10 y<br>• 67% at 2.5 y | All treatments combined:<br>• 71% in 31 d<br>• 62% at last follow-up |

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| Study | Interventions | | Survival | Off TPN |
|---|---|---|---|---|
| | Treatment | n | | |
| Rutter et al (2016)[10] | • Isolated IT<br>• Multivisceral graft<br>• Modified multivisceral | 16<br>35<br>9 | • 92% at 1 y; 37% at 5 y<br>• 71% at 1 y; 33% at 5 y<br>• 85% at 1 y; 65% at 5 y | NR |
| Lauro et al (2014)[11] | • Isolated IT<br>• Combined liver IT<br>• Multivisceral graft | 34<br>6<br>6 | All transplantations combined:<br>• 77% at 1 y<br>• 58% at 3 y<br>• 53% at 5 y<br>• 37% at 10 y | NR |
| Varkey et al (2013)[12] | • Isolated IT<br>• Combined liver IT<br>• Multivisceral graft | 4<br>1<br>15 | All transplantations combined:<br>• 78% at 1 y<br>• 50% at 5 y | NR |
| Mangus et al (2013)[4] | • Multivisceral graft<br>• Modified multivisceral | 84<br>16 | All transplantations combined:<br>• 72% at 1 y<br>• 57% at 5 y | NR |

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

**Complications**

Several case series have focused on complications after small bowel and multivisceral transplantation. For example, Nagai et al (2016) reported on cytomegalovirus (CMV) infection after intestinal or multivisceral transplantation at a single center in the United States.[13] 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. 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 multivisceral transplantation developed CMV infection a mean of 139 days (range, 14-243 days) postoperatively.[14]

Wu et al (2016) investigated the incidence and risk factors of acute antibody-mediated rejection (ABMR) among patients undergoing intestinal transplantation (N=175).[15] 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

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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.[16] 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.[17] 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.[18] 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 most 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]).

**HIV-Positive Transplant Recipients**

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

Current OPTN policy permits HIV-positive transplant candidates.[19]

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The British HIV Association and the British Transplantation Society (2017) updated their guidelines on kidney transplantation in patients with HIV disease.[20] 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 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, these case series have 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 Test 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 PICOTS were used to select literature to inform this review.

#### *Patients*

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.

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### *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.

### *Timing*

Periprocedural complications, short- and long-term graft survival, and 1- and 5-year OS are of interest.

### *Setting*

Retransplantation of small bowel, liver, or multivisceral transplantation takes place in a tertiary hospital setting.

### 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.[6] 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, (Range), mo |
|---|---|---|---|---|---|---|
| | | | | Treatment | n | |
| Ekser et al (2018)[21] | U.S. | 18[b] | 27.0 (17.4)[a] (0.9 to 57) | • Isolated IT<br>• Modified MVT<br>• Multivisceral graft | 1<br>1<br>16 | NR |
| Lacaille et al (2017)[7] | France | 10 | 13 (5-16) | • Isolated IT<br>• Combined liver IT | 3<br>7 | 4 |
| Desai et al (2012)[6] | U.S. | • 72 (adults)<br>• 77 (children) | NR | Adults:<br>• Isolated IT<br>• Combined liver IT<br>Children:<br>• Isolated IT | <br>41<br>31 | NR |

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| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | • Combined liver IT | 28<br>49 | |
| Abu-Elmagd et al (2009)[5] | U.S. | 47 | NR | • Isolated IT<br>• Combined liver IT<br>• Multivisceral graft | 31<br>7<br>9 | NR |
| Mazariegos et al (2008)[22] | U.S. | 14 | 9.4 (3.2-22.7) | • Isolated IT<br>• Combined liver IT<br>• Multivisceral graft | 1<br>3<br>10 | 55.9 |

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

**Table 4. Summary of Key Case Series Results for Retransplantations**

| Study | Interventions | | Survival | Off TPN |
|---|---|---|---|---|
| | Treatment | n | | |
| Ekser et al (2018)[21] | • Isolated IT<br>• Modified MVT<br>• Multivisceral graft | 1<br>1<br>16 | Graft survival:<br>• 71% at 1 y; 56% at 3 y; 44% at 5 y<br>Patient survival:<br>71% at 1 y; 47% at 3 y; 37% at 5 y | NR |
| Lacaille et al (2017)[7] | • Isolated IT<br>• Combined liver IT | 3<br>7 | All transplantations combined:<br>• 30% at last follow-up | NR |
| Desai et al (2012)[6] | Adults:<br>• Isolated IT<br>• Combined liver IT<br>Children:<br>• Isolated IT<br>• Combined liver IT | <br>41<br>31<br><br>28<br>49 | Adults:<br>• 80% at 1 y; 47% at 3 y; 29% at 5 y<br>• 63% at 1 y; 56% at 3 y; 47% at 5 y<br>Children:<br>• 81% at 1 y; 74% at 3 y; 57% at 5 y<br>• 42% at 1 y; 42% at 3 y; 42% at 5 y | NR |
| Abu-Elmagd et al (2009)[5] | • Isolated IT<br>• Combined liver IT<br>• Multivisceral graft | 31<br>7<br>9 | All transplantations combined:<br>• 69% at 1 y<br>• 47% at 5 y | NR |
| Mazariegos et al (2008)[22] | • Isolated IT<br>• Combined liver IT | 1<br>3<br>10 | All transplantations combined:<br>• 71% at last follow-up | 100% |

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| Study | Interventions | | Survival | Off TPN |
|---|---|---|---|---|
| | Treatment | n | | |
| | • Multivisceral graft | | | |

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

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

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## PRACTICE GUIDELINES AND POSITION STATEMENTS

### American Gastroenterological Association

The American Gastroenterological Association (2003) published a position statement on short bowel syndrome and intestinal transplantation.[23] 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

The American Society of Transplantation (2001) issued a position paper on indications for pediatric intestinal transplantation.[24] 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.

## ONGOING AND UNPUBLISHED CLINICAL TRIALS

A search of ClinicalTrials.gov in June 2018 did not identify any ongoing or unpublished trials that would likely influence this review.

## CODING

**The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. 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.**

CPT/HCPCS

44120 Enterectomy, resection of small intestine; single resection and anastomosis

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| | |
|---|---|
| 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, or 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]) |

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| | |
|---|---|
| 47145 | 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 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 |
| 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 Diagnoses (Effective October 1, 2015)

| | |
|---|---|
| K72.00 | Acute and subacute hepatic failure without coma |
| K72.01 | Acute and subacute hepatic failure with coma |
| K76.2 | Central hemorrhagic necrosis of liver |
| K72.10 | Chronic hepatic failure without coma |
| K72.11 | Chronic hepatic failure with coma |
| K72.90 | Hepatic failure, unspecified without coma |
| K72.91 | Hepatic failure, unspecified with coma |
| K91.2 | Postsurgical malabsorption, not elsewhere classified |

| **REVISIONS** | |
|---|---|
| 01-26-2010 | Policy added to the bcbsks.com web site. |
| 02-25-2010 | In Definition Section:<br>Updated definition of multivisceral transplant to: "…multivisceral transplant, which includes the small bowel and liver with 1 or more of the following organs: stomach, duodenum, jejunum, ileum, pancreas, and/or colon." |
| 02-10-2011 | Description section updated |
| | In Policy section:<br>▪ Revised wording of "evidence of impending end stage liver failure" to "other end stage organ failure"<br>▪ Removed criteria requiring "long term management with total parenteral nutrition (TPN)"<br>▪ Removed Policy Guidelines |

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| **REVISIONS** | |
|---|---|
| | Rationale section updated |
| | References section updated |
| 07-19-2011 | Rationale section updated |
| | In Coding section:<br>Updated wording for CPT Codes: 44121, 44721, 47135, 47136, 47141, 47142, 47144, 47145, 47147 |
| | References section updated |
| 11-19-2012 | Description section updated |
| | In Policy section:<br>▪ Created a Policy Guideline section<br>▪ Moved multivisceral definition from Description section to Policy Guideline section |
| | Rationale section updated |
| | In Coding section:<br>▪ Added CPT codes 44132, 44133<br>▪ Updated Diagnosis nomenclature |
| | References updated |
| 02-28-2014 | In Coding section:<br>▪ ICD-10 Diagnoses codes added |
| 01-01-2015 | In Coding section:<br>▪ Revised CPT Codes: 44799 (Effective January 1, 2015) |
| 11-13-2017 | Policy published 10-13-2017. Policy effective 11-13-2017. |
| | Description section updated |
| | In Policy section:<br>▪ In Item A added "Transplants, such as", "who have been managed with long-term total parenteral nutrition and who have developed evidence of impending", and "liver" and removed "other" and "organ" to read "Transplants, such as a multivisceral transplant and a small bowel and liver transplant may be considered medically necessary for pediatric and adult patients with intestinal failure (characterized by loss of absorption and the inability to maintain protein-energy, fluid, electrolyte, or micronutrient balance) who have been managed with long-term total parenteral nutrition and who have developed evidence of impending end-stage liver failure"<br>▪ Added Item B "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."<br>▪ Added Item C "A small bowel and liver transplant or multivisceral transplant is considered experimental / investigational in all other situations."<br>In Policy Guidelines:<br>▪ Removed "Definition<br>Regarding multivisceral transplants, a visceral organ is defined as any organ within the chest or abdomen. Stedman's states that visceral organ is from the viscera, the plural of viscus. The viscus is, "an organ of the digestive, respiratory, urogenital, and endocrine system as |

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| **REVISIONS** | |
|---|---|
| | well as the spleen, the heart, and great vessels; hollow and multilayered, walled organs studied in splanchnology." [Latin: the soft parts, internal organs] (Medical Director decision of 08/07/07.)" |
| | Rationale section updated |
| | In Coding section:<br>▪ Removed CPT code: 47136<br>▪ Added CPT code: 47399 |
| | References updated |
| 11-07-2018 | Description section updated |
| | In Policy section:<br>▪ Updated Policy Guidelines |
| | Rationale section updated |
| | References updated |

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