I. Description

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

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 case series. Relevant outcomes are overall survival, morbid events, and treatment-related mortality and morbidity. These procedures are infrequently performed and only relatively small case series, generally single-center, are available. These series have shown reasonably high postprocedural survival rates. Given exceedingly poor survival rates without transplantation of patients who have exhausted other treatments, evidence of postoperative survival from uncontrolled studies is sufficient to demonstrate that small bowel/liver and multivisceral transplantation provides a survival benefit in appropriately selected patients. Transplantation is contraindicated for patients in whom the procedure is expected to be futile due to comorbid disease or in whom 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 has suggested reasonably high survival rates. Given exceedingly poor survival rates without retransplantation of patients who have exhausted other treatments, evidence of postoperative survival from uncontrolled studies is sufficient to demonstrate that retransplantation provides a survival benefit in appropriately selected patients.
Retransplantation is contraindicated for patients in whom the procedure is expected to be futile due to comorbid disease or in whom 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.

Background
Small bowel transplants are typically performed in patients with short bowel syndrome, defined as an inadequate absorbing surface of the small intestine due to extensive disease or surgical removal of a large portion of small intestine. In some instances, short bowel syndrome is associated with liver failure, often due to the long-term complications of total parenteral nutrition (TPN). These patients may be candidates for a small bowel/liver transplant or a multivisceral transplant, which includes the small bowel and liver with 1 or more of the following organs: stomach, duodenum, jejunum, ileum, pancreas, and/or colon. A multivisceral transplant is indicated when anatomic or other medical problems preclude a small bowel/liver transplant.

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.

II. Policy
A. A small bowel/liver transplant or multivisceral transplant is covered (subject to Administrative Guidelines) 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 (TPN) and who have developed evidence of impending end-stage liver failure.

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

III. Policy Guidelines
GENERAL
A. Potential contraindications to solid organ transplant (subject to the judgment of the transplant center):
   1. Known current malignancy, including metastatic cancer
   2. Recent malignancy with high risk of recurrence
   3. History of cancer with a moderate risk of recurrence
   4. Systemic disease that could be exacerbated by immunosuppression
   5. Untreated systemic infection making immunosuppression unsafe, including chronic infection
   6. Other irreversible end-stage disease not attributed to intestinal failure
   7. Psychosocial conditions or chemical dependency affecting ability to adhere to therapy
B. 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 (adapted from reference 1). Short bowel syndrome is one case of intestinal failure.

C. Candidates should meet the following criteria:
- Adequate cardiopulmonary status
- Documentation of patient compliance with medical management

D. HIV [human immunodeficiency virus]-positive patients who meet the following criteria, as stated in the 2001 guidelines of the American Society of Transplantation, could be considered candidates for small bowel/live or multivisceral transplantation:
- CD4 count > 200 cells per cubic millimeter for greater than 6 months
- HIV-1 RNA undetectable
- On stable anti-retroviral therapy > 3 months
- No other complications from AIDS [acquired immune deficiency syndrome] (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidiosis mycosis, resistant fungal infections, Kaposi’s sarcoma, or other neoplasm), and meeting all other criteria for transplantation

SMALL BOWEL/LIVER SPECIFIC
A. Evidence of intolerance of total parenteral nutrition (TPN) includes, but is not limited to, multiple and prolonged hospitalizations to treat TPN-related complications, or the development of progressive but reversible liver failure. In the setting of progressive liver failure, small bowel transplant may be considered a technique to avoid end-stage liver failure related to chronic TPN, thus avoiding the necessity of a multivisceral transplant.

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

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<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>44120</td>
<td>Enterectomy, resection of small intestine; single resection and anastomosis</td>
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<tr>
<td>44121</td>
<td>;each additional resection and anastomosis</td>
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<tr>
<td>44132</td>
<td>Donor enterectomy (including cold preservation), open; from cadaveric donor</td>
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<tr>
<td>44133</td>
<td>;partial, from living donor</td>
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<tr>
<td>44715</td>
<td>Backbench standard preparation of cadaver or living donor intestine allograft prior to transplantation, including mobilization and fashioning of the superior mesenteric artery and vein</td>
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<td>HCPCS Code</td>
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<tr>
<td>S2053</td>
<td>Transplantation of small intestine, and liver allografts</td>
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<tr>
<td>S2054</td>
<td>Transplantation of multivisceral organs</td>
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<tr>
<td>S2055</td>
<td>Harvesting of donor multivisceral organs, with preparation and maintenance of allografts; from cadaver donor</td>
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ICD-10 codes are provided for your information. These will not become effective until the ICD-10 compliance date.

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<tr>
<th>ICD-10-CM</th>
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<tr>
<td>S2053</td>
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V. Scientific Background

This policy is updated regularly with searches of the MEDLINE database. The most recent literature search was through October 25, 2016.

TRANSPLANTATION OF SMALL BOWEL/LIVER OR MULTIVISCERAL ORGANS

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

“Multivisceral transplantation in patients with small bowel syndrome, liver failure, and/or other gastrointestinal problems such as pancreatic failure, thromboses of the celiac axis and the superior mesenteric artery, or pseudo-obstruction affecting the entire gastrointestinal tract 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.”

The published literature consists of case series, mainly reported by single centers. Authors of these reports, as well as reviews, observe that while outcomes continue to improve, recurrent and chronic rejection and complications of immunosuppression continue to be obstacles to long-term survival.

Among recent publications is a 2016 report by Rutter et al from the United Kingdom. Between January 2007, and June 2015, 60 transplant procedures were performed in 54 patients. Of these, 35 were multivisceral transplants, 9 were modified multivisceral transplants, and 16 were small bowel transplants. Recipients’ median age was 47 years (range, 18-61 years). Median length of follow-up was 21.3 months (range, 0-95 months). One- and 5-year patient survival rates were 77% and 62%, respectively. One-year survival by type of procedure was 71% for multivisceral transplant, 85% for modified multivisceral transplant, and 92% for small bowel transplant. Five-year survival rates in these groups were 33%, 65% and 83%, respectively. Most deaths occurred in the first year after transplant.
A 2014 single-center Italian case series reported on 45 patients who received either intestinal transplants alone or a combined transplant procedure. Twelve patients had small bowel/multivisceral transplants. Five of them had the procedure due to short-bowel syndrome, 2 due to chronic intestinal pseudo-obstruction, and 5 due to Gardner syndrome. Survival rates for the entire patient population were 77% at 1 year, 58% at 3 years, 53% at 5 years, and 37% at 10 years.

A 2013 single-center study in Sweden included 30 patients accepted for intestinal and multivisceral transplantation. One- and 3-year survival rates were 68% and 61%, respectively. Among patients awaiting transplantation after being accepted as candidates, there was a 34% survival rate.

Also in 2013, Mangus et al reported on 95 patients who underwent multivisceral transplantation with or without liver transplantation at a single U.S. center. One-year patient survival rate was 72% and 3-year survival was 57%. Authors noted a learning curve, with a 48% survival rate for transplants performed between 2004 and 2007 and a 70% survival rate for operations between 2008 and 2010.

Complications

Several case series have focused on complications after small bowel and multivisceral transplantation. For example, in 2016, Nagai et al reported on cytomegalovirus (CMV) infection after intestinal or multivisceral transplantation at a single center in the United States. A total of 210 patients had an intestinal transplant, multivisceral transplant, or modified multivisceral transplant between January 2003 and June 2014. Median length of follow-up was 2.1 years. Thirty-four (16%) patients developed CMV infection a median of 347 days after transplantation. Nineteen patients had tissue invasive CMV disease. In a report from another U.S. center, 16 (19%) of 85 patients undergoing intestinal or multivisceral transplantation developed CMV infection a mean of 139 days (range, 14-243 days) postoperatively.

In 2011 Wu et al reported on 241 patients who underwent intestinal transplantation. Of these, 147 (61%) had multivisceral transplants, 65 (27%) had small bowel transplants, and 29 (12%) had small bowel/liver transplants. There were 151 (63%) children and 90 (37%) adults. Twenty-two (9%) patients developed graft-versus-host disease (GVHD). Children younger than 5 years old were more likely to develop this condition; the incidence in this age group was 16 (13.2%) of 121 compared with 2 (6.7%) of 30 in children between 5 and 18 years and 9 (4.4%) of 90 in adults older than 18 years. In a 2016 series by Cromvik et al, 5 (19%) of 26 patients were diagnosed with GVHD after intestinal or multivisceral transplantation. Risk factors for GVHD were malignancy as a cause of transplantation and neoadjuvant chemotherapy or brachytherapy before transplantation.
A 2012 study retrospectively reported on bloodstream infections among 98 children (>18 years) with small bowel/combined organ transplants. Seventy-seven (79%) underwent small bowel transplant in combination with a liver, kidney or kidney and pancreas, and 21 had an isolated small bowel transplant. After a median follow-up of 52 months, 58 (59%) patients had survived. The 1-year survival rate was similar in patients with combined small bowel transplant (75%) and those with isolated small bowel transplant (81%). In the first year after transplantation, 68 (69.4%) patients experienced at least 1 episode of bloodstream infection. The 1-year survival rate for patients with bloodstream infections was 72% compared with 87% in patients without bloodstream infections (p=0.056 for difference in survival in patients with and without bloodstream infections).

**HIV-Positive Transplant Recipients**

No studies reporting on outcomes in HIV-positive patients who received small bowel/liver or multivisceral transplants were identified in literature reviews.

In 2001, the Clinical Practice Committee of the American Society of Transplantation proposed that the presence of AIDS could be considered a contraindication to kidney transplant unless the following criteria were present. (10) These criteria may be extrapolated to other organs:

- CD4 count greater than 200 cells/mm-3 for more than 6 months
- HIV-1 RNA undetectable
- On stable antiretroviral therapy for more than 3 months
- No other complications from AIDS (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidiose mycosis, resistant fungal infections, Kaposi’s sarcoma, or other neoplasm).
- Meeting all other criteria for transplantation.

In 2006, the British HIV Association and the British Transplantation Society Standards Committee published guidelines for kidney transplantation in patients with HIV disease. (11) As previously described, these criteria may be extrapolated to other organs. The guidelines, which are similar to those cited here, recommend that any patient with end stage organ disease with a life expectancy of at least 5 years is considered appropriate for transplantation under the following conditions:

- CD4 greater than 200 cells/mL for at least 6 months
- Undetectable HIV viremia (<50 HIV-1 RNA copies/mL) for at least 6 months
- Demonstrable adherence and a stable HAART regimen for at least 6 months
- Absence of AIDS-defining illness following successful immune reconstitution after HAART.

The 2013 the HIV Organ Policy Equity (HOPE) Act in the United States permitted scientists to research organ donations from a person with HIV to another HIV-infected person. In 2015, the Organ Procurement and Transplant Network (OPTN) updated its policies to be consistent with the HOPE Act. OPTN and United Network for Organ Sharing policies specify that organs from HIV-positive patients be used only for HIV-positive transplant recipients.

**Section Summary: Transplantation of Small Bowel/Liver or Multivisceral Organs**
These transplantation procedures are infrequently performed and only relatively small case series, generally single-center, are available. These series have shown a reasonably high posttransplant survival rates. Guidelines and U.S. federal policy no longer view HIV infection as an absolute contraindication for solid organ transplantation.

**RETRANSPLANTATION OF SMALL BOWEL/LIVER OR MULTIVISCERAL ORGANS**

In 2013, Trevizol et al reviewed literature on intestinal and multivisceral retransplantation. The authors found articles from 2 centers. Mazariegos et al reported on 15 retransplantations in 14 pediatric patients. By the end of follow-up, 4 patients had died and 10 patients had a normal graft function. TPN was weaned at a mean of 32 days after retransplantation. A 2009 study by Abu-Elmagd et al, discussed earlier, reported 47 retransplants after 500 intestinal and multivisceral transplantations in adults and children. Included were 31 intestinal retransplants, 9 multivisceral retransplants, and 7 intestinal/liver retransplants. For all types of retransplants combined, there is a 5-year survival rate of 47% for all retransplants.

Desai et al reported intestinal retransplantation data from the Organ Procurement and Transplant Network (OPTN) database. Between October 1987 and August 2009, there were 31 cases of small bowel/liver retransplants in adults and 49 in children. Among adults, 1-, 3-, and 5-year survival rates after retransplantation were 63.1%, 56.1%, and 46.8%, respectively. This compares with survival rates after primary small bowel/liver transplants of 67%, 53.3%, and 46% at 1-, 3- and 5-years. Among children, there was a 42.1% survival rate at 1-, 3- and 5 years after retransplantation. Survival rates after primary small bowel/liver transplantation was 67.6%, 56.1%, and 51.4%, respectively.

**Section Summary: Retransplantation of Small Bowel/Liver or Multivisceral Organs**

Data from only a small number of patients undergoing retransplantation are available. Although limited in quantity, the available data after retransplantation have suggested reasonably high survival rates after small bowel/liver 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 case series. Relevant outcomes are overall survival, morbid events, and treatment-related mortality and morbidity. These procedures are infrequently performed and only relatively small case series, generally single-center, are available. These series have shown reasonably high postprocedural survival rates. Given exceedingly poor survival rates without transplantation of patients who have exhausted other treatments, evidence of postoperative survival from uncontrolled studies is sufficient to demonstrate that small bowel/liver and multivisceral transplantation provides a survival benefit in appropriately selected patients. Transplantation is contraindicated for patients in whom the procedure is expected to be futile due to comorbid disease or in whom 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 has suggested reasonably high survival rates. Given exceedingly poor survival rates without retransplantation of patients who have exhausted other treatments, evidence of postoperative survival from uncontrolled studies is sufficient to demonstrate that retransplantation provides a survival benefit in appropriately selected patients. Retransplantation is contraindicated for patients in whom the procedure is expected to be futile due to comorbid disease or in whom 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.

SUPPLEMENTAL INFORMATION

PRACTICE GUIDELINES AND POSITION STATEMENTS

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

MEDICARE NATIONAL COVERAGE
Medicare covers intestinal transplantation for the purposes of restoring intestinal function in patients with irreversible intestinal failure only when performed for patients who have failed total parenteral nutrition and only when performed in centers that meet approved criteria. The criteria for approval of centers will be based on an annual volume of 10 intestinal transplants per year with a 1-year actuarial survival rate of 65% (these criteria were affirmed in 2006).

VI. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.
Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

VII. References


