Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for Small Bowel/Liver and Multivisceral Transplant when it is determined to be medically necessary because the criteria shown below are met.

**When Policy Topic is covered**

A small bowel/liver transplant or multivisceral 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 (TPN) and who have developed evidence of impending end-stage liver failure.

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

**When Policy Topic is not covered**

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

**Considerations**

**General**

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

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). (1) Short bowel syndrome is one case of intestinal failure.

Candidates should meet the following criteria:

- Adequate cardiopulmonary status
- Documentation of patient compliance with medical management.

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/liver or multivisceral transplantation:

- CD4 count greater than 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**

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.

**Transplant Benefit**

Small bowel/liver or multivisceral transplants should be considered for coverage under the transplant benefit.

What is covered under the scope of the human organ transplant (HOT) benefit needs to be considered. Typically, the following are covered under the HOT benefit:

- hospitalization of the recipient for medically recognized transplants from a donor to a transplant recipient;
- prehospital workup and hospitalization of a living donor undergoing a partial hepatectomy should be considered as part of the recipient transplant costs;
- evaluation tests requiring hospitalization to determine the suitability of both potential and actual donors, when such tests cannot be safely and effectively performed on an outpatient basis;
- hospital room, board, and general nursing in semiprivate rooms;
▪ special care units, such as coronary and intensive care;
▪ hospital ancillary services;
▪ physicians’ services for surgery, technical assistance, administration of anesthetics, and medical care;
▪ acquisition, preparation, transportation, and storage of organ;
▪ diagnostic services;
▪ drugs that require a prescription by federal law.

Expenses incurred in the evaluation and procurement of organs and tissues are benefits when billed by the hospital. Included in these expenses may be specific charges for participation with registries for organ procurement, operating rooms, supplies, use of hospital equipment, and transportation of the tissue or organ to be evaluated.

Administration of products with a specific transplant benefit needs to be defined as to:
▪ when the benefit begins (at the time of admission for the transplant or once the patient is determined eligible for a transplant, which may include tests or office visits before transplant);
▪ when the benefit ends (at the time of discharge from the hospital or at the end of required follow-up, including the immunosuppressive drugs administered on an outpatient basis).

Coverage usually is not provided for:
▪ HOT services for which the cost is covered/funded by governmental, foundational, or charitable grants;
▪ organs sold rather than donated to the recipient;
▪ an artificial organ.

**Description of Procedure or Service**

Small bowel/liver transplantation is transplantation 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.

Evidence for small bowel/liver and multivisceral transplant and retransplant consists of case series. Though infrequently performed, the transplant procedures are demonstrated to provide a survival benefit, and the procedure is considered medically necessary for patients who have been managed with long-term total parenteral nutrition and who have developed evidence of impending end-stage liver failure.

**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.

**Note:** Isolated small bowel transplants are considered in a separate policy.

**Rationale**

This policy was originally created in 1995 and was updated regularly with searches of the MEDLINE database. The most recent literature review was conducted through May 4, 2015.

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.²

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

In 2010, Nayyar et al reported that there had been improvements in 5-year actuarial patient and graft survival after liver/small bowel transplant since the use of rabbit antithymocyte globulin induction began to be used in their pediatric center in 2002 (81% vs 58% and 76% vs 52%, respectively).³ In addition to innovations in immunosuppressive therapy, the authors cited new approaches to management of short gut syndrome including hypoallergenic formulas and modification of enteral nutrition to prevent total parenteral nutrition (TPN)‒induced cholestasis. The authors noted that better understanding of the protective role of the liver in preventing chronic rejection of the small bowel allograft could improve long-term survival after isolated small bowel transplantation.

Other survival data include a 2009 report by Abu-Elmagd et al reporting on their experience with 500 intestinal and multivisceral transplantations.⁴ The study found 1- and 5-year patient survival of 92% and 70%, respectively. A 2013 study from a single center in Sweden included 30 patients accepted for intestinal and multivisceral transplantation.⁵ 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. In 2013, Mangus et al reported on 95
patients who underwent multivisceral transplantation with or without liver transplantation at 1 site in the United States. One-year patient survival was 72% and 3-year survival was 57%. The 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.

Several case series have focused on complications after small bowel and multivisceral transplantation. For example, 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 12% had small bowel/liver transplants. There were 151 children (63%) and 90 adults. A total of 22 patients (9%) developed graft-versus-host disease. Children younger than 5 years old were more likely to develop this condition; the incidence in this age group was 16 of 121 (13.2%) compared with 2 of 30 (6.7%) in children between 5 and 18 years and 9 of 90 (4.4%) in adults older than 18 years. In addition, a 2012 article retrospectively reported on bloodstream infections among 98 children younger than age 18 years with small bowel/combined organ transplants. Seventy-seven (79%) patients underwent small bowel transplant in combination with a liver, kidney or kidney-pancreas, and 21 had an isolated small bowel transplant. After a median follow-up of 52 months, 58 (59%) patients remained alive. 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 patients (69.4%) 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).

A 2014 single-center Italian case series reported on transplants in 45 patients who received either intestinal transplants alone or a combined transplant procedure. Twelve of the patients had small bowel/multivisceral transplants. Five of these had the procedure due to short-bowel syndrome, 2 had chronic intestinal pseudo-obstruction, and 5 had 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.

**HIV-Positive Transplant Recipients**

This subgroup of recipients has long been controversial, due to the long-term prognosis for HIV positivity and the impact of immunosuppression on HIV disease. Although HIV-positive transplant recipients may be a research interest of some transplant centers, the minimal data regarding long-term outcome in these patients primarily consist of case reports and abstract presentations of liver and kidney recipients. Nevertheless, some transplant surgeons would argue that HIV positivity is no longer an absolute contraindication to transplant due to the advent of highly active antiretroviral therapy, which has markedly changed the natural history of the disease. 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. 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 (eg, opportunistic infection, including aspergillus, tuberculosis, coccidioses 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. 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.

Furthermore, as of November 2010, the United Network for Organ Sharing policy on identification of transmissible diseases in organ recipients states, “A potential candidate for organ transplantation whose test for HIV is positive should not be excluded from candidacy for organ transplantation unless there is a documented contraindication to transplantation based on local policy.”

No studies that reported on outcomes in HIV-positive patients who received small bowel/liver or multivisceral transplants have been identified in literature reviews.

**Retransplantation**

In 2012, Trevizol et al published a review of literature from the previous 5 years 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 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.

Ongoing and Unpublished Clinical Trials
A search of ClinicalTrials.gov in May 2015 did not identify any ongoing or unpublished trials that would likely influence this policy.

Summary of Evidence
Evidence for small bowel/liver and multivisceral transplant and retransplant consists of case series. Though infrequently performed, the transplant procedures are demonstrated to provide a survival benefit, and the procedure is considered medically necessary for patients who have been managed with long-term total parenteral nutrition and who have developed evidence of impending end stage liver failure.

Practice Guidelines and Position Statements
No relevant guidelines or position statements were identified.

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

Medicare National Coverage
Medicare will cover 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 of 65% (these criteria were reviewed again in 2006 and upheld).

References

### Billing Coding/Physician Documentation Information

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>44120</td>
<td>Enterectomy, resection of small intestine; single resection and anastomosis</td>
</tr>
<tr>
<td>44121</td>
<td>Enterectomy, resection of small intestine; each additional resection and anastomosis (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>44132</td>
<td>Donor enterectomy (including cold preservation), open; from cadaver donor</td>
</tr>
<tr>
<td>44133</td>
<td>Donor enterectomy (including cold preservation), open; partial, from living donor</td>
</tr>
<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>
</tr>
<tr>
<td>44720</td>
<td>Backbench reconstruction of cadaver or living donor intestine allograft prior to transplantation; venous anastomosis, each</td>
</tr>
<tr>
<td>44721</td>
<td>Backbench reconstruction of cadaver or living donor intestine allograft prior to transplantation; arterial anastomosis, each</td>
</tr>
<tr>
<td>44799</td>
<td>Unlisted procedure, intestine</td>
</tr>
</tbody>
</table>
47133  Donor hepatectomy (including cold preservation), from cadaver donor
47135  Liver allotransplantation; orthotopic, partial or whole, from cadaver or living donor, any age
47136  Liver allotransplantation; heterotopic, partial or whole, from cadaver or living donor, any age (code deleted 1/1/2016)
47140  Donor hepatectomy (including cold preservation), from living donor; left lateral segment only (segments II and III)
47141  Donor hepatectomy (including cold preservation), from living donor; total left lobectomy (segments II, III and IV)
47142  Donor hepatectomy (including cold preservation), from living donor; total right lobectomy (segments V, VI, VII and VIII)
47143  Backbench standard preparation of cadaver donor whole liver graft prior to allotransplantation, including cholecystectomy, if necessary, and dissection and removal of surrounding soft tissues to prepare the vena cava, portal vein, hepatic artery, and common bile duct for implantation; without trisegment or lobe split
47144  Backbench standard preparation of cadaver donor whole liver graft prior to allotransplantation, including cholecystectomy, if necessary, and dissection and removal of surrounding soft tissues to prepare the vena cava, portal vein, hepatic artery, and common bile duct for implantation; with trisegment split of whole liver graft into two partial liver grafts (ie, left lateral segment (segments II and III) and right trisegment (segments I and IV through VIII))
47145  Backbench standard preparation of cadaver donor whole liver graft prior to allotransplantation, including cholecystectomy, if necessary, 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 two partial liver grafts (ie, 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
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 Codes
K72.00- Acute and subacute hepatic failure code range
K72.01
K72.10- Chronic hepatic failure code range
K72.11
K91.2  Postsurgical malabsorption, not elsewhere classified (includes short bowel syndrome)
## Additional Policy Key Words

N/A

## Policy Implementation/Update Information

<table>
<thead>
<tr>
<th>Date</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/1/01</td>
<td>New policy. Added to the surgery section.</td>
</tr>
<tr>
<td>11/1/02</td>
<td>No policy statement changes. Added to the transplant section.</td>
</tr>
<tr>
<td>11/1/03</td>
<td>No policy statement changes. Added new HCPCPS codes.</td>
</tr>
<tr>
<td>11/1/04</td>
<td>Policy statement revised to include HIV+ status as investigational.</td>
</tr>
<tr>
<td>11/1/05</td>
<td>Policy statement revised to remove HIV+ status as investigational.</td>
</tr>
<tr>
<td>4/1/06</td>
<td>No policy statement changes. Added general criteria to the considerations section.</td>
</tr>
<tr>
<td>11/1/06</td>
<td>No policy statement changes.</td>
</tr>
<tr>
<td>11/1/07</td>
<td>No policy statement changes.</td>
</tr>
<tr>
<td>11/1/08</td>
<td>No policy statement changes.</td>
</tr>
<tr>
<td>11/1/09</td>
<td>No policy statement changes.</td>
</tr>
<tr>
<td>11/1/10</td>
<td>No policy statement changes.</td>
</tr>
<tr>
<td>11/1/11</td>
<td>Policy statement revised to list absolute contraindications as not medically necessary.</td>
</tr>
<tr>
<td>11/1/12</td>
<td>Contraindications combined (absolute and relative) and moved to Considerations section. Wording of contraindications changed to be consistent with other solid organ transplant policies.</td>
</tr>
<tr>
<td>11/1/13</td>
<td>Statement added that small bowel/liver transplant or multivisceral retransplant may be considered medically necessary after a failed primary small bowel/liver transplant or multivisceral transplant.</td>
</tr>
<tr>
<td>11/1/14</td>
<td>Statement revised that procedure is investigational in all other situations. (previously considered not medically necessary.</td>
</tr>
<tr>
<td>11/1/15</td>
<td>No policy statement changes.</td>
</tr>
<tr>
<td>11/1/16</td>
<td>No policy statement changes.</td>
</tr>
</tbody>
</table>

State and Federal mandates and health plan contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The medical policies contained herein are for informational purposes. The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents Blue KC and are solely responsible for diagnosis, treatment and medical advice. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, photocopying, or otherwise, without permission from Blue KC.