



Kansas City

An Independent Licensee of the Blue Cross and Blue Shield Association

## Isolated Small Bowel Transplant

**Policy Number:** 7.03.04

**Last Review:** 2/2014

**Origination:** 11/2001

**Next Review:** 2/2015

### **Policy**

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Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for a small bowel transplant when it is determined to be medically necessary because the criteria shown below are met.

### **When Policy Topic is covered**

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A small bowel transplant using cadaveric intestine may be considered **medically necessary** in adult and pediatric patients with intestinal failure (characterized by loss of absorption and the inability to maintain protein-energy, fluid, electrolyte, or micronutrient balance), who have established long-term dependency on total parenteral nutrition (TPN) and are developing or have developed severe complications due to 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.

### **When Policy Topic is not covered**

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A small bowel transplant is considered **investigational** for adults with intestinal failure who are able to tolerate TPN.

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

### **Considerations**

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#### **General**

Potential contraindications subject to the judgment of the transplant center:

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

#### **Small Bowel Specific**

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.

Patients who are developing or have developed severe complications due to 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 above 3 mg/dl) is often associated with 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.

Small bowel transplants should be considered for coverage under the Transplant Benefit.

### **Transplant Benefit**

The date on which the Transplant Benefit starts accumulating is determined by the transplant coordinator. The Transplant Benefit ends when the Transplant Lifetime Maximum benefit (if applicable) has been exhausted.

Benefits include:

- hospitalization of the recipient for medically recognized transplants from a donor to a transplant recipient;
- evaluation tests requiring hospitalization to determine the suitability of both potential (member's benefits must be verified with regard to the potential donor who does not turn out to be the actual donor) and actual donors, when such tests cannot be safely and effectively performed on an outpatient basis (**Note:** The member's benefits must be verified with regard to the **potential** donor who does not turn out to be the **actual** donor.);
- hospital room, board and general nursing in semi-private 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 / tissue / cells;
- diagnostic services;
- drugs which require a prescription by federal law;
- medical and surgical care of the donor (related to the procurement of the organ / tissue / cells) if coverage is not available to the donor from any other source. (Covered services provided to a donor will be applied against the recipient's transplant maximum benefit, if applicable)

If the donor and recipient are both listed on the same (family) policy, BCBSKC charges only one deductible and one coinsurance, if applicable.

In addition to the specific organ criteria, transplant candidates must also meet the following general criteria, including, but not limited to:

- Since compliance is a major factor in transplant graft survival, the patient (or legal guardian) must have the ability to accept and understand the transplant procedure and to maintain compliance with long-term medical management and immunosuppression.
- If applicable, patients with a history of malignancy must have passed the recommended length of time to be considered cured for that specific cancer. A complete metastatic evaluation must be performed before a patient will be considered an acceptable transplant candidate.
- Patients with a history of alcohol or substance abuse must have a six month history of abstinence as evidenced by negative urine or serum drug screens taken randomly.
- The patient must have adequate cardiopulmonary status.
- The patient must be free from active infection.

A covered person is eligible for retransplantation as deemed medically necessary and appropriate by Blue Cross and Blue Shield of Kansas City (Blue KC). Review of a retransplantation request will include review of the covered person's compliance with relevant transplant selection criteria including,

but not limited to, adherence to medication regimens, follow-up examinations and abstinence from the use of alcohol and drugs.

The specific member contract should be reviewed for coverage related to donors and recipients, out of network treatment, drugs and other possible limitations or exclusions.

Coverage will not be provided for:

- Transplant services for which the cost is covered/funded by governmental, foundation, or charitable grants;
- organs sold rather than donated to the recipient;
- an artificial organ.

Clinical trials for conditions other than those allowed in this policy may be available in the research setting. However, these trials are considered investigational and/or experimental and therefore contract exclusions.

*Note: There are some state mandates in place that require insurance carriers to cover certain clinical trials under very specific guidelines. Please contact your BCBSKC representative for more information.*

Due to the special nature of this procedure, this transplant may require an out of network exception.

### **Description of Procedure or Service**

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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. When the small bowel and liver are transplanted in conjunction with other gastrointestinal organs, the procedure is referred to as a multivisceral transplant. Small bowel/liver transplants and multivisceral transplants are considered in a separate policy (see Related Policy).

### **Background**

A small bowel transplant is typically performed in patients with short bowel syndrome. This 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 small intestine. In adults, etiologies of short bowel syndrome include ischemia, trauma, volvulus, and tumors. In children, gastroschisis, volvulus, necrotizing enterocolitis, and congenital atresias are predominant causes.

The small intestine, particularly the ileum, does have the capacity to 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 is focused on achieving adequate macro- and micro-nutrient 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). Patients with complications from TPN may be considered candidates for 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 recent interest in using living donors.

Intestinal transplants (including multivisceral and bowel/liver) represent a small minority of all solid organ transplants. In 2011, 129 intestinal transplants were performed in the United States, of which all but 1 was from deceased donors. (1)

### **Rationale**

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#### **Literature Review**

This policy is based on 1995 and 1999 TEC Assessments. The 1995 Assessment concluded that in children, small bowel transplant was associated with improved survival compared to total parenteral

nutrition (TPN) as the associated adverse outcomes for small bowel transplant were offset by severe TPN-related complications. (3) This Assessment also concluded that, in adults, the outcomes for small bowel transplant were worse than that associated with TPN. A 1999 TEC Assessment reevaluated the data on adults and concluded that it is not possible to predict which patients would survive longer on TPN versus small bowel transplant and therefore that transplantation is a reasonable option in selected adults. (4)

This policy has been regularly updated with searches of the MEDLINE database. The most recent literature search was for the period from August 2012 through August 15, 2013. Much of the published literature consists of case series reported by single centers. These reports, as well as reviews of the reports, observe that while outcomes continue to improve, obstacles to long-term survival remain. Recurrent and chronic rejections and complications of immunosuppression are significant issues in bowel transplantation.

One issue in the literature is the importance of timely referral for intestinal transplantation to avoid the necessity of combined liver and intestine transplantation. (5) It has been suggested that recent improvements in survival may justify removing the restriction of intestinal transplantation to patients who have severe complications of TPN. However, as noted by Vianna and colleagues in their 2008 report on the status of intestinal transplantation, no randomized trials compare intestinal transplantation to long-term parenteral nutrition, and optimal timing for earlier transplantation has not been established. (6) This review also noted that the currently reported 1-year graft and patient survival rate for intestinal transplantation was 80%.

Another issue in the literature is the rate of various complications after small bowel transplant. Florescu and colleagues have published several articles retrospectively reviewing complications in a cohort of 98 pediatric patients. Twenty-one of these children (21.4%) had an isolated small bowel transplant; the remainder had combined transplants. A 2012 study reported that 68 of the 98 patients (69%) developed at least one episode of bloodstream infection. (7) Among the patients with an isolated small bowel transplant, the median time to infection for those who became infected was 4.5 months (95% confidence interval [CI]: 2.4-6.7 months). Also in 2012, the researchers reported that 7 of 98 patients (7%) developed cytomegalovirus (CMV) disease; only 1 of these had an isolated small bowel transplant. (8) In 2010, Florescu and colleagues reported that 25 of 98 cases reviewed (25.5%) developed at least one episode of fungal infection; *Candida* infection was most common. (9) The mortality rate did not differ significantly between patients who did and did not develop a fungal infection (32.3% vs. 29.8%, respectively;  $p=0.46$ ). In 2013, a research group in France reported that 7 of 12 children who had an isolated small bowel transplant had renal function complications at some point after surgery. (10) Prior to treatment, all of the patients had normal renal functioning.

#### *Living donors*

Cadaveric intestines have been most commonly used, but recently there has been 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. Small case reports have been published of 1 or 2 patients with different lengths of the ileum or jejunum. (11-14) While there appear to be minimal complications to the donors, of the 6 cases reported, 5 recipients remain on TPN for at least part of their nutrition. One patient remains healthy and is off TPN.

Benedetti and colleagues reported outcomes from 4 children and 7 adults who underwent 12 living-related small bowel transplantations between 1998 and 2004. (15) All donors were reported to have had uneventful recovery following removal of up to 40% of the small intestine. The 3-year patient survival was 82%, with graft survival of 75%. Longer follow-up from the earlier cases was not reported. Gangemi and Benedetti published a literature review of living donor small bowel transplantation reports from 2003 to 2006; all of the reports listed Benedetti (et al.) as author. (16) The authors comment that, "Due to the excellent result in modern series of deceased donor bowel transplantation, widespread use

of the procedure [living donor] should not be recommended, in consideration of the potential risks to donor. Furthermore, few centers have acquired the necessary experience with the procedure.”

In June 2010, Sudan published a review of current literature on long-term outcomes after intestinal transplantation. (17) In this paper, the author notes that intestinal transplantation has become standard therapy for patients with life-threatening complications from parenteral nutrition therapy. Data from current single-center series indicates a 1-year patient survival rate of 78-85% and a 5+ year survival rate of 56-61%. With respect to pediatric intestinal transplant patients, the majority achieve normal growth velocity at 2 years posttransplant. However, oral aversion is a common problem; tube feedings are necessary in 45% of children. Sudan also reports on parental surveys of quality of life in pediatric transplant patients in which intestinal transplant patients appear to have modestly improved quality of life compared to patients remaining on TPN and slightly worse than matched school-age controls without intestinal disease.

#### *HIV+ transplant recipients*

This subgroup of recipients has long been controversial, due to the long-term prognosis for human immunodeficiency virus (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 (HAART), which has markedly changed the natural history of the disease.

As of February 2013, the United Network for Organ Sharing (UNOS) policy on HIV-positive transplant candidates 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.” (Policy 4, Identification of Transmissible Diseases in Organ Recipients). (18)

In 2006, the British HIV Association and the British Transplantation Society Standards Committee published guidelines for kidney transplantation in patients with HIV disease. (19) As described above, these criteria may be extrapolated to other organs.

The guidelines, which are similar to those cited above, 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 200 cells/micro liter 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.

#### **Clinical Input Received through Physician Specialty Societies and Academic Medical Centers**

In response to requests, input was received through 2 physician specialty societies and 2 academic medical centers while this policy was under review for July 2009. 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. The consensus of those providing input was that small bowel transplant should be performed in patients who are developing severe TPN-related complications and that small bowel transplant from living donors may be considered when cadaveric intestinal transplants are not available.

#### **Summary**

Based on the evidence review and clinical input, small bowel transplant may be considered medically necessary in patients with intestinal failure who are developing severe total parenteral nutrition-related

complications, to obviate the subsequent need for a multivisceral transplant. Small bowel transplantation using a living donor may be considered medically necessary only when a cadaveric intestinal transplant is not available. Routine use of living-donor intestinal transplants is considered not medically necessary because the net health outcome associated with this procedure is reduced (compared to cadaveric transplant) because of donor-related morbidity.

### **Practice Guidelines and Position Statements**

In 2003, the American Gastroenterological Association produced a medical position statement on short bowel syndrome and intestinal transplantation. It recommends dietary, medical, and surgical solutions. Indications for intestinal transplantation mirror those of CMS. The guidelines acknowledge the limitations of transplant for these patients. (20)

### **Medicare National Coverage**

Effective for services performed on or after April 1, 2001, this procedure is covered only when performed for patients who have failed total parenteral nutrition (TPN) and only when performed in centers that meet approval criteria. (21)

#### *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. The clinical manifestations include elevated serum bilirubin and/or liver enzymes, splenomegaly, thrombocytopenia, gastroesophageal varices, coagulopathy, stomal bleeding or hepatic fibrosis/cirrhosis.
- Thrombosis of the major central venous channels; jugular, subclavian, and femoral veins. Thrombosis of two or more of these vessels is considered a life-threatening complication and failure of TPN therapy. The sequelae of central venous thrombosis are lack of access for TPN infusion, fatal sepsis due to infected thrombi, pulmonary embolism, Superior Vena Cava syndrome, or chronic venous insufficiency.
- Frequent line infection and sepsis. The development of two or more episodes of systemic sepsis secondary to line infection per year that requires hospitalization indicates failure of TPN therapy. A single episode of line-related fungemia, septic shock and/or Acute Respiratory Distress Syndrome are considered indicators of TPN failure.
- Frequent episodes of severe dehydration despite intravenous fluid supplement in addition to TPN. Under certain medical conditions such as secretory diarrhea and nonconstructable gastrointestinal tract, the loss of the gastrointestinal and pancreaticobiliary secretions exceeds the maximum intravenous infusion rates that can be tolerated by the cardiopulmonary system. Frequent episodes of dehydration are deleterious to all body organs particularly kidneys and the central nervous system with the development of multiple kidney stones, renal failure, and permanent brain damage.

#### *2. Approved Transplant Facilities*

Intestinal transplantation is covered by Medicare if performed in an approved facility. The criteria for approval of centers will be based on a volume of 10 intestinal transplants per year with a 1-year actuarial survival of 65 percent using the Kaplan-Meier technique.

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### **Billing Coding/Physician Documentation Information**

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| <b>44132</b> | Donor enterectomy (including cold preservation), open; from cadaver donor  |
| <b>44133</b> | Donor enterectomy (including cold preservation), open; partial, from living donor  |
| <b>44135</b> | Intestinal allotransplantation; from cadaver donor   |
| <b>44136</b> | Intestinal allotransplantation; from living donor  |
| <b>44715</b> | Backbench standard preparation of cadaver or living donor intestine allograft prior to transplantation, including mobilization and fashioning of the superior mesenteric artery and vein |
| <b>44720</b> | Backbench reconstruction of cadaver or living donor intestine allograft prior to transplantation; venous anastomosis, each   |
| <b>44721</b> | Backbench reconstruction of cadaver or living donor intestine allograft prior to transplantation; arterial anastomosis, each   |

### **Additional Policy Key Words**

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N/A

### **Policy Implementation/Update Information**

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| 11/1/01 | New policy added to the Surgery section.                      |
| 11/1/02 | No policy statement changes. Added to the transplant section. |

11/1/03	No policy statement changes.
11/1/04	Policy statement revised to include HIV+ status as investigational.
11/1/05	Policy statement revised to remove HIV+ status as investigational.
4/1/06	No policy statement changes. Added general criteria to the considerations section
11/1/06	No policy statement changes.
11/1/07	No policy statement changes.
11/1/08	No policy statement changes.
11/1/09	Policy statements changed to indicate the small bowel transplant may be considered medically necessary in those developing severe TPN-related complications, and that small bowel transplants from living donors may be considered medically necessary only when cadaveric transplants are not available. The word "isolated" was added to the title.
11/1/10	No policy statement changes.
11/1/11	No policy statement changes.
11/1/12	Potential contraindications added to Policy Guidelines. Wording of potential contraindications consistent with other solid organ transplant policies
2/1/14	Added A small bowel retransplant may be considered medically necessary after a failed primary small bowel transplant.

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