Cigna Medical Coverage Policy

Subject: Intestinal and Multivisceral Transplantation

Effective Date: 4/15/2014
Next Review Date: 4/15/2015
Coverage Policy Number: 0288

Hyperlink to Related Coverage Policies
- Liver Transplantation
- Nutritional Support

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna companies. Coverage Policies are intended to provide guidance in interpreting certain standard Cigna benefit plans. Please note, the terms of a customer’s particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer’s benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer’s benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations. Proprietary information of Cigna. Copyright ©2014 Cigna

Coverage Policy

Cigna covers primary and repeat deceased donor intestinal transplantation and primary and repeat deceased donor multivisceral organ transplantation in an individual with total irreversible intestinal failure as medically necessary for ANY of the following indications:

- failure, contraindication, or intolerance to parenteral nutrition with ANY of the following:
  - impending or overt liver failure
  - impending loss of central vein access (e.g., thrombosis)
  - recurrent, life-threatening sepsis
  - frequent episodes of dehydration
- high risk of death
- severe short bowel syndrome
- frequent hospitalizations
- pseudo-obstruction

Cigna does not cover deceased donor intestinal or multivisceral transplantation when ANY of the following absolute contraindications to transplantation exist because it is considered not medically necessary (this list may not be all-inclusive):

- malignancy that is expected to significantly limit future survival
- unsuccessfully treated major or systemic infections
- systemic illness or comorbidities that would be expected to substantially negatively impact the successful completion and/or outcome of transplant surgery
• a pattern of demonstrated patient noncompliance which would place a transplanted organ at serious risk of failure
• human immunodeficiency virus (HIV) disease unless ALL of the following are noted:
  ➢ CD4 count greater than 200 cells/mm³
  ➢ HIV-1 ribonucleic acid (RNA) undetectable
  ➢ stable anti-retroviral therapy for more than three months
  ➢ absence of serious complications associated with or secondary to HIV disease (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidioidomycosis; resistant fungal infections; or Kaposi’s sarcoma or other neoplasm)

Cigna does not cover living donor intestinal or multivisceral transplantation for any indication because it is considered experimental, investigational or unproven.

General Background

Intestinal (i.e., small bowel only), liver-intestinal, or multivisceral transplantation are accepted therapeutic options for highly selected individuals with irreversible intestinal and/or multivisceral organ failure who have failure, contraindication, or intolerance to total parenteral nutrition (TPN). Irreversible gastrointestinal system failure is defined as the inability to maintain nutrition or adequate fluid and electrolyte balance without special support, when currently available medical and surgical treatments fail to improve intestinal adaptation and gut function. Causes may differ among children and adults (Matarese, 2006). Although TPN is the standard of care for patients with temporary or permanent intestinal failure, it severely affects quality of life and may be associated with a number of highly morbid and sometimes fatal complications and has a treatment-related mortality of 7–28% (Markman, 2012). Transplantation should be considered once it has been clearly shown that the bowel cannot adapt to allow full enteral autonomy from parenteral nutrition (Braun, 2007). Additional life-threatening indications include impending or overt liver failure, loss or impending loss of central venous access (e.g., thrombosis), recurrent, systemic sepsis, frequent episodes of dehydration, high risk of death, severe short bowel syndrome, frequent hospitalization, or pseudo-obstruction (Reyes, 2011; Avitzur, 2010; Centers for Medicare and Medicaid Services [CMS], 2006; American Gastroenterological Society [AGA], 2003, Kaufman, 2001).

Specific indications for intestinal and multivisceral transplantation may include the following (Sudan, 2012; Reyes, 2011; Lauro, 2007; Reyes, 2007; Carter, 2006; Matarese, 2006; Dove and Brown, 2004; AGA, 2003; Abu-Elmagd, 2001):

**Common Indications for Intestinal and Multivisceral Transplantation**

<table>
<thead>
<tr>
<th>Children</th>
<th>Adults</th>
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</thead>
<tbody>
<tr>
<td>Aganglionosis (Hirschsprung’s disease)</td>
<td>Autoimmune enteritis</td>
</tr>
<tr>
<td>Autoimmune enteropathy</td>
<td>Crohn’s disease</td>
</tr>
<tr>
<td>Congenital epithelial mucosal disease (microvillus inclusion disease, tufting enteropathy)</td>
<td>Desmoid tumors</td>
</tr>
<tr>
<td>Familial polyposis</td>
<td>Gardner’s syndrome/familial polyposis</td>
</tr>
<tr>
<td>Gastrochisis</td>
<td>Hollow visceral myopathy</td>
</tr>
<tr>
<td>Inflammatory pseudotumor</td>
<td>Inflammatory bowel disease</td>
</tr>
<tr>
<td>Intestinal atresia</td>
<td>Ischemia</td>
</tr>
<tr>
<td>Intestinal failure-associated liver disease</td>
<td>Radiation enteritis</td>
</tr>
<tr>
<td>Intestinal pseudo-obstruction</td>
<td>Secretory diarrhea</td>
</tr>
<tr>
<td>Microvillus inclusion disease</td>
<td>Short gut syndrome</td>
</tr>
<tr>
<td>Necrotizing enterocolitis</td>
<td>Surgical adhesions</td>
</tr>
<tr>
<td>Pseudo-obstruction</td>
<td>Trauma</td>
</tr>
<tr>
<td>Radiation enteritis</td>
<td>Vascular occlusion</td>
</tr>
<tr>
<td>Short gut syndrome</td>
<td>Volvulus</td>
</tr>
<tr>
<td>Tufting enteropathy</td>
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</tbody>
</table>
Intestinal and multivisceral transplantations are more challenging than other types of solid organ transplantation due to the intestine’s large number of immune competent cells and colonization of the gut with microorganisms. Intestinal allografts may be transplanted alone, as in an isolated intestine graft, or as a composite graft which may include the liver, duodenum, and pancreas. If the recipient operation includes replacement of the entire gastrointestinal graft, and liver it is generally referred to as a multivisceral transplantation (Reyes, 2011). The type and number of transplanted organs is dictated by the extent of the abdominal pathology and the functional status of the organs at the time of transplantation (Abu-Elmagd, 2006; Matarese, 2006).

Isolated intestine transplantation may be indicated when there is a permanent need for total parenteral nutrition (TPN) after failure of intestinal adaptation, and attempts of medical and surgical rehabilitation (Matarese, 2006). Combined liver-intestinal transplantation may be appropriate for individuals with combined intestinal and TPN-associated liver failure, liver failure associated with portal and mesenteric venous thrombosis, intestinal failure due to a hypercoagulable state associated with enzyme deficiencies that can be corrected by a liver graft (e.g., mesenteric vascular thrombosis secondary to protein C or S deficiency), or documented end-stage hepatic disease. In adults, such disease is associated with refractory ascites, spontaneous bacterial peritonitis, refractory variceal bleeding, chronic encaphalopathy, hepatorenal syndrome, failure to thrive, or a severe compromise in the quality of life (Abu-Elmagd, 2001). In children, end-stage hepatic disease is suggested by hyperbilirubinemia persisting beyond three to four months of age, combined with features of portal hypertension, such as splenomegalay, thrombocytopenia, or prominent superficial abdominal veins.

A full multivisceral transplantation involves the en bloc transplantation of the stomach, liver, duodenum and pancreas with the intestine. In a modified procedure only one or two organs may be transplanted. It is indicated for patients with irreversible failure of their abdominal visceral organs, including the small bowel. The aims of multivisceral transplantation are to replace as many functional digestive units as possible, restore gastric emptying, ileocecal valve function, rectal continence, and improvement of surgical and oncological margins of resection (Braun, 2007). Conditions include symptomatic extensive thrombosis of the splanchnic vascular system, massive gastrointestinal polyposis or neoplasm, and generalized hollow visceral myopathy or neuropathy (Abu-Elmagd, 2001). Multivisceral transplantation may also be indicated for diffuse gastrointestinal disorders such as dysmotility syndromes, hereditary neoplasms, and extensive vascular thrombosis (Matarese, 2006). According to Organ Procurement and Transplant Network annual report data (2011), almost 50% of deceased donor intestines were transplanted with another organ in 2011. In 2011, this organ was most commonly the pancreas.

Contraindications to Intestinal and Multivisceral Transplantation

Contraindications for intestinal and multivisceral transplantation are similar to those for other types of solid organ transplantation. Absolute contraindications include severe uncontrolled infection, multiorgan failure, nonresectable or disseminated malignancy, significant cardiopulmonary insufficiency, acquired immunodeficiency syndrome, the existence of life-threatening uncontrollable intra-abdominal or systemic infections, and noncompliance (Braun, 2007; Matarese, 2006; Abu-Elmagd, 2001; Kaufman, 2001). In addition to the absolute contraindications noted, relative contraindications which may also negatively affect survival, may include, but not be limited to (Kaufman, 2007; Abu-Elmagd, 2001):

- current, ongoing substance abuse, including tobacco, alcohol and narcotic/other addictive pain medications
- profound neurologic disabilities
- severe congenital or acquired immunological deficiencies
- multisystem autoimmune diseases
- progressive neuropathy or myopathy that is not amenable to rehabilitation
- any active medical process that is currently not optimally treated and/or stable and that is likely to result in end-organ damage or medical emergency without appropriate management, such as active peptic ulcer disease, diverticular disease, active hepatitis, cholecystitis, pancreatitis, diabetes mellitus, hypertension, autoimmune disease, or cytopenia
- advanced age
- positive cross-match
Deceased (Cadaver) Donor Intestinal and Multivisceral Transplantation

Intestinal and multivisceral transplantations most frequently involve the use of cadaveric, or deceased, donors. Although randomized clinical trial data are not available, there are several case reports and retrospective studies demonstrating improved outcomes. According to national data from the Organ Procurement Transplant Network (OPTN), one-, three-, and five-year patient survival outcomes for individuals undergoing initial or primary deceased donor intestinal transplantation from 1996-2004 (as of March 7, 2014) are 79.8%, 60.7%, and 47.3%, respectively. Neither graft nor patient survival data are available for multivisceral transplantation from the OPTN.

Literature Review

Abu-Elmagd et al. (2009) reported results of a retrospective review of 453 patients who received 500 visceral transplants at a single transplant facility. Of 453 recipients, 198 (44%) received intestine, 142 (31%) received combined liver-intestine, and 113 (25%) received multivisceral grafts: 84 with liver (full) and 29 without liver (modified). Actuarial patient survival was 85% at 1-year, 61% at 5-years, 42% at 10-years, and 35% at 15-years with respective graft survival of 80%, 50%, 33%, and 29%. With a 10% retransplantation rate, second/third graft survival was 69% at 1-year and 47% at 5-years. Although limited by uncontrolled study design, long-term survival data suggest acceptable overall survival rates for primary and repeat intestinal and multivisceral transplantation.

Living Donor Intestinal and Multivisceral Transplantation

The use of living intestine donors remains controversial (Benedetti, 2006). Potential advantages to the use of living donors may be the application of desensitization protocols to improve outcomes, reduced waiting times, better human leukocyte antigen matching, and the setting of an elective procedure. Major limitations of this technique include risks to the donor and the potential inferior physiologic performance of the segmental graft compared to a full postmortal graft (Braun, 2007). Questions remain regarding donor risks, including long-term complications of bowel resection and potential impairment of intestinal absorption. Other issues include optimum drainage system, choice of segment of the intestine for transplantation and timing and closure of the ostomy (Ontario Medical Advisory Secretariat, 2003).

Data are limited in the published peer-reviewed scientific literature regarding the safety and improvement in health outcomes with living donors for intestinal or multivisceral transplantation. Published results of case reports and retrospective reviews are limited by small participant numbers, study methods, and a lack of long-term donor and recipient outcomes. Longer follow-up is needed to better assess the safety and effectiveness of this procedure. At this time there is insufficient evidence to support living donor intestinal or multivisceral transplantation for any indication. Although results appear promising, the role of living donor intestinal or multivisceral transplantation has not been established.

Literature Review

Gangemi et al. (2009) retrospectively reported the results of 10 children who received a total of 13 living donor intestinal ([LDITx], n=8) or combined living donor intestinal and liver transplantations ([CLDLITx], n=5). In this study, one- and three-year patient and graft survival rates for LDITx were 60% and 50%, respectively. For recipients of CLDLITx, one- and two-year patient survival were 100%, liver graft survival was 100%, and bowel graft survival was 80%. Study limitations that preclude the ability to generalize outcomes to the general population include uncontrolled study design and small participant numbers.

Retransplantation

The overall effect of intestinal and multivisceral retransplantation in the United States has not been evaluated in a comprehensive manner and there are limited data in the published, peer-reviewed medical literature. Causes of graft loss may include acute cellular rejection, chronic rejection, post transplant lymphoproliferative disorder, graft dysmotility or dysfunction, severe infection, arterial graft aneurysm, or allograft liver failure (Mazariegos, 2008). Careful patient selection, post transplant immunosuppression, and patient management are essential for successful long-term outcomes (Mazariegos, 2008). Based on Organ Procurement Transplant Network ([OPTN] data for repeat intestine transplants performed between 1997-2004 Kaplan-Meier one-, three-, and five-year patient survival rates (as of Mar 7, 2014) were 64.1%, 39.8%, and 47.7%, respectively. Individuals undergoing repeat intestinal or multivisceral transplantation should meet all of the eligibility criteria for primary transplantation and should not have absolute contraindications to transplantation.
Literature Review
Desai et al. (2012) performed an analysis of United Network of Organ Sharing (UNOS) registry data relative to outcomes for intestine retransplantation performed in children and adults from 1987-2009. Of 1822 isolated intestine transplants (ITx) in 1664 patients during the study period, 149 patients (adults, n=72; children, n=77) received retransplants. Nine of these were third transplants, all in children. Of 41 adult isolated ITx, patient survival was 80.1%, 47.4%, and 28.5% at 1, 3, and 5 years, respectively, which is lower than outcomes seen with primary isolated ITx (p=0.005). For combined liver/ITx retransplantation in adults (L-ITx, n=31), patient survival at one-, three-, and five-years was 63.1%, 56.1%, and 46.8%, respectively, compared with primary L-ITx retransplantation (p=0.07). Isolated ITx retransplantation in children (n=28) resulted in patient survival of 80.7%, 74%, and 57.5% at one-, three-, and five-years, respectively. One-, three-, and five-year patient survival in children receiving L-ITX was 42%, 42%, and 42%, respectively. Although data suggests lower survival rates for retransplantation compared to primary transplantation, outcomes are acceptable in this population of individuals for which alternative treatment options are limited.

Professional Societies/Organizations
American Society of Transplantation (AST): On behalf of the AST, Kaufman (2001) published guidelines regarding the indications for pediatric intestinal transplantation. These include progressive parenteral nutrition-associated liver disease, recurring sepsis, impending loss of central venous access, extreme short-bowel syndrome, and congenital intractable epithelial (mucosal) disorders. The Society notes that intestinal transplantation is a lifesaving therapy for the child with intestinal failure. Transplantation should be considered when intestinal failure has been, or will probably become, refractory to conventional management, the mainstay of which remains parenteral nutrition therapy.

American Gastroenterological Association (AGA): The AGA’s medical position statement: Short Bowel Syndrome and Intestinal Transplantation (2003) notes the following indications for intestinal transplantation:
• impending or overt liver failure
• thrombosis of major central venous channels
• frequent central line-related sepsis
• frequent severe dehydration

Use Outside of the US
No relevant information.

Summary
Although randomized controlled trial data are lacking, published consensus guidelines and peer-reviewed scientific literature support deceased donor intestinal and multivisceral transplantation as accepted treatment for highly selected individuals with irreversible intestinal failure associated with high morbidity/mortality or a failure, contraindication or intolerance to parenteral nutrition (PN). Repeat intestinal or multivisceral transplantation may be appropriate for an individual who meets eligibility criteria for primary transplantation. Although promising, the role of living donor intestinal or multivisceral transplantation has not yet been established.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

Covered when medically necessary when used to report primary and repeat deceased donor intestinal transplantation and primary and repeat deceased donor multivisceral organ transplantation:

<table>
<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>44132</td>
<td>Donor enterectomy (including cold preservation), open; from cadaver donor</td>
</tr>
<tr>
<td>44135</td>
<td>Intestinal allotransplantation; from cadaver donor</td>
</tr>
<tr>
<td>44137</td>
<td>Removal of transplanted intestinal allograft, complete</td>
</tr>
<tr>
<td>44140</td>
<td>Colectomy, partial; with anastomosis</td>
</tr>
<tr>
<td>HCPCS Codes</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
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</tr>
<tr>
<td>S2053</td>
<td>Transplantation of small intestine and liver allografts</td>
</tr>
<tr>
<td>S2054</td>
<td>Transplantation of multivisceral organs</td>
</tr>
<tr>
<td>S2055</td>
<td>Harvesting of donor multivisceral organs, with preparation and maintenance of allografts; from cadaver donor</td>
</tr>
<tr>
<td>S2152</td>
<td>Solid organ(s), complete or segmental, single organ or combination of organs; deceased or living donor(s), procurement, transplantation, and related complications including: drugs; supplies; hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services; and the number of days of pre-and post-transplant care in the global definition</td>
</tr>
</tbody>
</table>

Experimental/Investigational/Unproven/Not Covered when used to report living donor intestinal or multivisceral organ transplantation for any indication:

Page 6 of 12
Coverage Policy Number: 0288
### CPT® Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>44133</td>
<td>Donor enterectomy (including cold preservation), open; partial, from living donor</td>
</tr>
<tr>
<td>44136</td>
<td>Intestinal allotransplantation; from living donor</td>
</tr>
<tr>
<td>44137</td>
<td>Removal of transplanted intestinal allograft</td>
</tr>
<tr>
<td>44140</td>
<td>Colectomy, partial; with anastomosis</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>47135</td>
<td>Liver allotransplantation; orthotopic, partial or whole, from cadaver or living donor, any age</td>
</tr>
<tr>
<td>47136</td>
<td>Liver allotransplantation; heterotopic, partial or whole, from cadaver or living donor, any age</td>
</tr>
<tr>
<td>47140</td>
<td>Donor hepatectomy (including cold preservation), from living donor; left lateral segment only (segments II and III)</td>
</tr>
<tr>
<td>47141</td>
<td>Donor hepatectomy (including cold preservation), from living donor; total left lobectomy (segments II, III and IV)</td>
</tr>
<tr>
<td>47142</td>
<td>Donor hepatectomy (including cold preservation), from living donor; total right lobectomy (segments V, VI, VII and VIII)</td>
</tr>
<tr>
<td>47146</td>
<td>Backbench reconstruction of cadaver or living donor liver graft prior to allotransplantation; venous anastomosis, each</td>
</tr>
<tr>
<td>47147</td>
<td>Backbench reconstruction of cadaver or living donor liver graft prior to allotransplantation; arterial anastomosis, each</td>
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<tr>
<td>48550</td>
<td>Donor pancreatectomy (including cold preservation), with or without duodenal segment for transplantation</td>
</tr>
<tr>
<td>48554</td>
<td>Transplantation of pancreatic allograft</td>
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</tbody>
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### HCPCS Codes

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**References**


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