Liver Transplantation

Coverage Policy

Liver transplantation is considered medically necessary for an individual with ANY of the following indications:

- end-stage liver failure
- hepatocellular carcinoma (i.e., single lesion ≤ 5 cm, up to three separate lesions, none larger than 3 cm, no evidence of gross vascular invasion and no regional nodal metastasis)
- hepatoblastoma which is confined to the liver (children)
- metabolic disease with intact hepatic synthetic function (e.g., type I hyperoxaluria, familial homozygous hypercholesterolemia, familial amyloidosis)
- unresectable hilar cholangiocarcinoma when the individual has received a Model for End-Stage Liver Disease (MELD) score exception by a United Network for Organ Sharing (UNOS) Regional Review Board for all of the following considerations:
  - a UNOS approved treatment protocol
  - mass ≤3cm on imaging studies
  - absence of metastasis
  - completion of neoadjuvant therapy
  - subsequent operative staging
- neuroendocrine/gastroenteropancreatic (GEP) tumors with ALL of the following:
  - unresectable liver metastasis
  - prior complete resection of the primary GEP
  - absence of extrahepatic metastasis
  - failure to respond to medical and/or interventional treatment

Related Coverage Resources

Transplantation Donor Charges
severe hypoglycemia, poorly controlled hyperglycemia, cardiac distress, respiratory distress or other symptoms directly attributable to aberrant GEP tumor production of life-threatening hormones such as insulin, catecholamines, or histamine

Liver retransplantation is considered medically necessary for an individual considered to have a significant chance of success and who still meet eligibility criteria for primary transplantation for ANY of the following indications:

- primary graft failure
- hepatic artery thrombosis
- severe rejection
- recurrence of the disease which prompted the initial liver transplantation

Liver transplantation is considered not medically necessary for an individual with ANY of the following contraindications to transplant surgery:

- ongoing alcohol abuse
- active extrahepatic malignancy that is expected to significantly limit future survival
- persistent, recurrent or 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 noncompliance which would place a transplanted organ at serious risk of failure
- human immunodeficiency virus (HIV) disease unless ALL of the following are noted:
  - cluster determinant (CD)4 count >100 cells/mm³
  - HIV-1 ribonucleic acid (RNA) undetectable
  - stable antiretroviral therapy for more than three months
  - absence of serious complications associated with HIV disease (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidioidomycosis; or resistant fungal infections; or Kaposi's sarcoma or other neoplasm)
- known intrahepatic or central cholangiocarcinoma
- donor with:
  - ongoing alcohol abuse
  - active malignancy, with the exception of non-melanotic skin cancer
  - persistent, recurrent or unsuccessfully treated infections, including hepatitis A, B or C or HIV
  - active systemic illness or serious comorbidities that would be expected to substantially negatively impact the successful completion and/or outcome of transplant surgery
  - active systemic illness that is likely to negatively affect survival

Overview

This Coverage Policy addresses liver transplantation.

General Background

In the United States, 130 programs perform about 6000 transplants per year, and about 17,000 patients are on waiting lists because recipients needing liver transplantation exceed the donor liver supply. The mortality rate while waiting on a list is 116 deaths per 1000 patient-years. Since 1982, patient survival after liver transplantation has steadily increased by 20 to 30%, whether it is measured at three months, one year, five years, or ten years, largely because of improvements within the first year after transplantation. The positive shift in survival during the first three months after transplantation is related to improvements in surgical techniques and immediate postoperative care (Everson, 2016).

Liver transplantation is a complex operation requiring vascular reconstruction of the hepatic artery, the portal vein, and the hepatic venous system. Surgical techniques, which continue to evolve, include the orthotopic approach, involving replacement of the recipient liver with the donor liver, and the heterotopic approach in which
the recipient liver is left in place and the donor liver is transplanted to an ectopic site. The whole liver, a reduced liver, or a liver segment may be transplanted depending on whether the donor is cadaveric (deceased) or living.

Living-donor liver transplantation was introduced as an alternative to deceased donor transplantation in response to the shortage of available cadaveric donor organs and is used for both adults and children. The graft from a living donor is more commonly from a relative of the recipient. The success of this type of transplantation is based on the ability of the liver to regenerate in both the donor and the recipient. The graft must be of adequate size in order to function in the recipient. The risks and benefits of using a living-donor graft must be considered as there are surgical risks to both the recipient and the donor. Benefits to the recipient include a reduced chance of mortality related to waiting for a cadaveric-donor organ, a reduced likelihood of primary non-function of the graft, and a potential decrease in the chance of graft rejection and the need for immunosuppression.

A major factor in patient survival following transplantation is the degree of hepatic decompensation and associated debility at the time of transplantation. Using the Model for End Stage Liver Disease (MELD) scoring model for an individual who is ≥12 years, and the Pediatric End-Stage Liver Disease (PELD) scoring model for a child <12 years, a donor organ is allocated to a transplant candidate designated as having the greatest risk of death. Exceptions to this policy, which result in the assignment of additional MELD/PELD points and therefore a higher priority for allocation of donor organs, can be requested of a United Network for Organ Sharing (UNOS) regional review board by the transplanting physician and/or facility for individuals with certain diagnoses.

Indications for Liver Transplantation
The most common indications for liver transplantation in the United States are hepatitis C virus (30%) and alcoholic liver disease (18%). Other indications include the following:
- Idiopathic/autoimmune liver disease (12%)
- Primary biliary cirrhosis (10%)
- Primary sclerosing cholangitis (8%)
- Acute liver failure (7%)
- Hepatitis B virus (6%)
- Metabolic liver disease (eg, inborn errors of metabolism) (3%)
- Cancer (3%)
- Other (3%)

Biliary atresia is a common indication for liver transplantation in pediatric patients.

The most common problems in the liver transplant recipient are the following:
- Acute graft rejection
- Vascular thrombosis
- Biliary leak or stricture
- Infection
- Malignancy
- Adverse effects of immunosuppressant drugs

Patients with hepatocellular carcinoma are candidates for liver transplantation unless they have large tumors, multicentric tumors, macrovascular invasion, or extrahepatic spread. Criteria used include Milan criteria and the University of California, San Francisco (UCSF) criteria. Cholangiocarcinoma, in the absence of underlying liver or biliary disease, typically is manifested in elderly patients with significant comorbidities and is not an indication for liver transplantation. By contrast, cholangiocarcinoma arising in younger patients with underlying biliary disease, such as primary sclerosing cholangitis, may be considered for transplantation if staging is negative for vascular, lymphatic, or neural invasion. The 2- and 5-year post-transplantation survivals of patients with cholangiocarcinoma limited to the perihilar region of the liver and treated with adjuvant chemoradiation are 78% and 65%, respectively (Everson, 2016).

Contraindications to Liver Transplantation
Many factors affect the outcome of solid organ transplantation. Prior to transplantation a rigorous assessment of the recipient’s medical status should be conducted to confirm that transplantation constitutes the best option for managing the patient’s disease and that no contraindications exist. According to the American Association for
the Study of Liver Diseases and the American Society of Transplantation (Martin, et al., 2014), these are listed contraindications to liver transplant:

- MELD Score <15
- Severe cardiac or pulmonary disease
- AIDS
- Ongoing alcohol or illicit substance abuse
- Hepatocellular carcinoma with metastatic spread
- Uncontrolled sepsis
- Anatomic abnormality that precludes liver transplantation
- Intrahepatic Cholangiocarcinoma
- Extrahepatic malignancy
- Fulminant hepatic failure with sustained intracranial pressure >50 mm Hg or cerebral perfusion pressure <40 mm Hg
- Hemangiosarcoma
- Persistent noncompliance
- Lack of adequate social support system

**Human Immunodeficiency Virus (HIV)**
Historically, HIV positivity has been considered a contraindication to solid organ transplantation. Access to liver transplantation was limited due to questions regarding life expectancy, clinical efficacy, and complications post-liver transplantation caused by interactions between antiviral therapy and immunosuppressive medications, and the increased risk of opportunistic infections.

More recently liver transplantation has become an acceptable treatment option for selected individuals who are HIV-positive. While overall survival is generally lower for individuals with HIV-infection compared to HIV-negative persons, monoinfection (i.e. HIV infection only) does not seem to be a significant risk factor for survival after liver transplantation. Orthotopic liver transplantation appears to be a safe therapeutic option in the short term for selected persons with HIV infection who have end-stage liver disease.

At present, AASLD criteria for liver transplantation include a CD 4 count >100/μL with a viral load anticipated to be completely suppressed at time of transplant.

**Donor Health**
The health of the donor is also an important factor in liver transplantation outcomes. Hepatitis C virus (HCV) infection in the donor can affect the health of the donor liver, making individuals with persistent, recurrent, or untreated HCV infection unacceptable donors. Likewise, donor candidates who are hepatitis B surface antigen (HbsAg) positive are also generally excluded from living-donor liver transplant donation to prevent transmission of disease to recipients. Factors which may negatively affect recipient outcomes after liver transplantation including ongoing alcohol abuse, active systemic illness, and malignancy, are also considered contraindications to donation.

**Retransplantation of the Liver**
Retransplantation may be appropriate for carefully selected patients experiencing graft loss if an improvement in survival is expected; however, liver retransplantation should be used with discretion in the emergency setting and avoided in patients with little chance of success. In adults, the most common condition resulting in the need for retransplantation of the liver is recurrent infection with hepatitis C virus (HCV). Retransplantation in patients with HCV is controversial due to concerns of aggressive disease recurrence post retransplantation, and decreased patient and graft survival. Several retrospective cohort studies have examined the outcomes of patients retransplanted for recurrent HCV demonstrating lower patient and graft survival in some studies.

**Professional Societies/Organizations**
American Association for the Study of Liver Disease (AASLD)/ American Society of Transplantation (AST): The AASLD and AST have published numerous joint guidelines, including some specific to liver transplantation.
Evaluation for Liver Transplantation in Adults: 2013 Practice Guideline by the AASLD and the American Society of Transplantation (Marin, et al., 2014) states liver transplantation (LT) is indicated for severe acute or advanced chronic liver disease when the limits of medical therapy have been reached. Recognition of cirrhosis per se does not imply a need for LT. Many patients with cirrhosis in the absence of an index complication such as ascites or variceal hemorrhage will not develop hepatic decompensation, although patients with cirrhosis have diminished survival compared to the population as a whole. Acute liver failure complications of cirrhosis include ascites, chronic gastrointestinal blood loss due to portal hypertensive gastropathy, encephalopathy, liver cancer, refractory variceal hemorrhage and synthetic dysfunction.

Evaluation of the Pediatric Patient for Liver Transplantation: 2014 Practice Guideline by the American Association for the Study of Liver Diseases, American Society of Transplantation and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (Squires, et al., 2014) indications for LT include biliary atresia (32%), metabolic/genetic conditions (22%), acute liver failure (11%), cirrhosis (9%), liver tumor (9%), immune-mediated liver and biliary injury (4%), and other miscellaneous conditions (13%). Within these broad categories rest many rare conditions with myriad presentations.

American Society of Transplantation (AST): The AST has several Key Position Statements, including but not limited to Deceased Organ Donation, Insurance Coverage for Living Donors, and Insurance Coverage for Transplant Recipients, and Living Organ Donation. They also publish guidelines, including Long-Term Medical Management of the Pediatric Patient after Liver Transplantation, Long-Term Management of the Successful Adult Liver Transplant, Curricular Guidelines for Training in Transplant Hepatology, and a Position paper on Indications for pediatric intestinal transplantation.

National Comprehensive Cancer Network Guidelines™ (NCCN Guidelines™): The NCCN Guidelines (1.2017) for Hepatobiliary Cancers states under Principles of Surgery that patients meeting the UNOS criteria (single lesion ≤5cm, or 2 or 3 lesions ≤3cm) should be considered for transplantation (cadaveric or living donation). More controversial are those patients whose tumor characteristic are marginally outside of the UNOS guidelines and may be considered at some institutions for transplantation. Patients with tumor characteristics beyond Milan criteria that are downstaged to within criteria can also be considered for transplantation. Patients with Child-Pugh Class A function, who fit UNOS criteria and are resectable, could be considered for resection or transplant. There is controversy over which initial strategy is preferable to treat such patients.

Organ Procurement & Transplantation Network (OPTN): In December 2017, the OPTN/UNOS Board of Directors approved a new policy to address geographic disparities in access to livers for organ transplant. The revised policy will offer more transplant access to candidates at a greater medical priority level who are local to the donor hospital, whether they are inside or outside current regional boundaries. The national board will replace the individual review boards in each of the 11 OPTN regions, creating greater consistency in assigning exception scores for medical conditions not assessed reliably by MELD or PELD scores.

The OPTN Policies document (OPTN, 2018) addresses Allocation of Livers and Liver-Intestines. Sections within the policy address many topics related to liver transplant including various indications for transplantation. The OPTN lists the following Liver Diagnosis Categories and associated Liver Diagnoses under Reasons for Liver Transplants on their website (not dated) under Organ Datasource:

Non-cholestatic Cirrhosis:
- Laennec's Cirrhosis (Alcoholic)
- Laennec's Cirrhosis and Postnecrotic Cirrhosis
- Cirrhosis: Postnecrotic--Type C
- Cirrhosis: Cryptogenic--Idiopathic
- Cirrhosis: Postnecrotic--Autoimmune-Lupoi
- Cirrhosis: Postnecrotic--Type B-Hbsag+
- Cirrhosis: Postnecrotic--Type Non A Non B
- Cirrhosis: Postnecrotic--Type B and C
- Cirrhosis: Postnecrotic--Other Specify
- Cirrhosis: Drug/Indust Exposure Other Specify
- Cirrhosis: Postnecrotic--Type B and D
• Cirrhosis: Postnecrotic--Type A
• Cirrhosis: Postnecrotic--Type D
• Cirrhosis: Postnecrotic--Chronic Active Hepatitis

Cholestatic Liver Disease/Cirrhosis:
• Primary Biliary Cirrhosis (PBC)
• Sec Biliary Cirrhosis: Other Specify
• Sec Biliary Cirrhosis: Caroli's Disease
• Sec Biliary Cirrhosis: Choledochol Cyst
• Choles Liver Disease: Other Specify
• Primary Sclerosing cholangitis: Other Specify
• Primary Sclerosing cholangitis: Ulcerative Colitis
• Primary Sclerosing cholangitis: No Bowel Disease
• Primary Sclerosing cholangitis: Crohn's Disease

Biliary Atresia:
• Biliary Atresia: Other Specify
• Biliary Atresia: Extrahepatic
• Biliary Atresia: Alagille's Syndrome
• Biliary Atresia: Hypoplasia

Acute Hepatic Necrosis (AHN):
• AHN: Etiology Unknown
• AHN: Type B- Hbsag+
• AHN: Drug Other Specify
• AHN: Non-A Non-B
• AHN: Type C
• AHN: Type A
• AHN: Other Specify
• AHN: Type B and C
• AHN: Type B and D
• AHN: Type D
• Hepatitis C: Chronic or Acute
• Hepatitis B: Chronic or Acute

Metabolic Diseases:
• Alpha-1-Antitrypsin Defic A-1-A
• Wilson's Disease
• Hemochromatosis-Hemosiderosis
• Other Specify
• Tyrosinemia
• Primary Oxalosis/Oxaluria-Hyper
• Glyc Stor Dis Type IV (GSD-IV)
• Glyc Stor Dis Type I (GSD-I)
• Hyperlipidemia-II-Homozygous Hy

Malignant Neoplasms:
• Primary Liver Malignancy: Hepatoma--Hepatocellular Carcinoma
• Primary Liver Malignancy: Hepatoma (HCC) and Cirrhosis
• Primary Liver Malignancy: Cholangiocarcinoma (CH-CA)
• Primary Liver Malignancy: Hepatoblastoma (HBL)
• Primary Liver Malignancy: Hemangioendothelioma-Hemangiosarcoma
• Primary Liver Malignancy: Other Specify
• Primary Liver Malignancy: Fibrolamellar (FL-HC)
• Bile Duct Cancer (Cholangioma-Biliary Tr)
- Secondary Hepatic Malignancy Other Specify

Other:
- Other Specify
- Cystic Fibrosis
- Budd-Chiari Syndrome
- TPN/Hyperalimentation Ind Liver Disease
- Neonatal Hepatitis Other Specify
- Congenital Hepatic Fibrosis
- Familial Cholestasis: Other Specify
- Familial Cholestasis: Byler's Disease
- Trauma Other Specify
- Graft vs. Host Dis Sec to Non-Li Tx
- Chronic or Acute
- Benign Tumor: Polycystic Liver Disease
- Benign Tumor: Other Specify
- Benign Tumor: Hepatic Adenoma

Use Outside of the US
European Association for the Study of the Liver (EASL): The EASL Clinical Practice Guidelines on Liver transplantation notes the following recommendations:

- Evaluation for liver transplantation (LT) should be considered when a major complication of cirrhosis occurs (Grade II-2*)
- MELD score is good to predict short-term pretransplant mortality risk (Grade II-1)
- MELD is based on objective laboratory tests and can be used in organ allocation (Grade II-1)
- As the MELD has several limitations, patients with liver diseases requiring LT, whose severity is not described by the MELD, should be recognized. A different priority needs to be given to these patients by experts (Grade II-3/III)
- HCC is a particular MELD exception that requires extra points to get access to the transplant. These points have to be standardized in each country and have to take into account size, number of nodules, AFP levels, recurrence after downstaging therapy (Grade II-1)
*Grade evidence:
I Randomized, controlled trials
II-1 Controlled trials without randomization
II-2 Cohort or case-control analytic studies
II-3 Multiple time series, dramatic uncontrolled experiments
III Opinions of respected authorities, descriptive epidemiology

National Institute for Clinical Excellence (NICE): A NICE guidance on Living-donor liver transplantation (November 2015) notes that “Current evidence on the efficacy and safety of living-donor liver transplantation appears adequate to support the use of this procedure for suitable donors and recipients with normal arrangements for clinical governance, consent and audit, provided that the necessary regulatory requirements are followed”.

Pediatric Gastroenterology Chapter of Indian Academy of Pediatrics/Indian Academy of Pediatrics (2013): A published consensus statement regarding the management of acute liver failure (ALF) in infants and children notes liver transplantation is the only definite treatment for ALF. Contraindications for pediatric liver transplantation are active uncontrollable and untreatable sepsis, severe cardiopulmonary disease, multi-organ failure, extrahepatic malignancy, mitochondrial disease, active substance abuse, and HE grade IV encephalopathy with severe neurological impairment.

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
Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

<table>
<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>47133</td>
<td>Donor hepatectomy (including cold preservation), from cadaver donor</td>
</tr>
<tr>
<td>47135</td>
<td>Liver allotransplantation, orthotopic, 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>47143</td>
<td>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</td>
</tr>
<tr>
<td>47144</td>
<td>Backbench standard preparation of cadaver donor whole liver graft prior to allotransplantation, including cholecystectomy, if necessary, and dissection and removal of surrounding soft tissues to prepare the vena cava, portal vein, hepatic artery, and common bile duct for implantation; with trisegment split of whole liver graft into 2 partial liver grafts (ie, left lateral segment [segments II and III] and right trisegment [segments I and IV through VIII])</td>
</tr>
<tr>
<td>47145</td>
<td>Backbench standard preparation of cadaver donor whole liver graft prior to allotransplantation, including cholecystectomy, if necessary, and dissection and removal of surrounding soft tissues to prepare the vena cava, portal vein, hepatic artery, and common bile duct for implantation; with lobe split of whole liver graft into 2 partial liver grafts (ie, left lobe [segments II, III, and IV] and right lobe [segments I and V through VIII])</td>
</tr>
<tr>
<td>47146</td>
<td>Backbench reconstruction of cadaver or living donor liver graft prior to allotransplantation; venous anastomosis, each</td>
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<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>47399</td>
<td>Unlisted procedure, liver</td>
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<th>HCPCS Codes</th>
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<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>
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References


