Anthem

Medical Policy

Subject: Liver Transplantation
Document #: TRANS.00008
Status: Reviewed

Publish Date: 01/03/2024
Last Review Date: 11/09/2023

Description/Scope

This document addresses liver transplantation for individuals with end-stage liver disease. Donor livers are obtained from deceased donors, in which a whole or partial (split) liver may be transplanted. Living donors are another possible source from adult to child or adult to adult.

Note: Please see the following for additional information:

- CG-TRANS-02 Kidney Transplantation
- TRANS.00013 Small Bowel, Small Bowel/Liver and Multivisceral Transplantation

Position Statement

Note: Members must meet the disease specific criteria as well as the general Individual Selection Criteria below for the transplantation to be considered medically necessary.

Medically Necessary:

A whole or partial liver transplant using a deceased or living donor is considered **medically necessary** for selected individuals with end-stage organ failure due to irreversible liver damage that includes, but is not limited to, the following conditions:

A. Cholestatic liver diseases:
   1. Primary biliary cirrhosis
   2. Primary sclerosing cholangitis
   3. Biliary atresia
   4. Caroli's disease
   5. Familial cholestasis
   6. Arteriohepatic dysplasia (Alagaille's disease)
   7. Cystic Fibrosis

B. Hepatocellular injury:
   1. Viral-induced Hepatitis
   2. Drug induced
      a. Acetaminophen
      b. Associated with halothane, gold, disulfram, others
   3. Alcohol induced
   4. Toxin exposure: Amanita mushroom poisoning
   5. Autoimmune hepatitis

C. Inborn errors of metabolism:
   1. Wilson's disease
   2. Organic acidurias
   3. Hemochromatosis
   4. Alpha-1 antitrypsin deficiency
   5. Homozygous type II hyperlipoproteinemia
   6. Crigler-Najjar Syndrome type I
   7. Protoporphyria
   8. Some urea cycle deficiencies
   9. Glycogen storage diseases types I and IV
   10. Tyrosine deficiency
   11. Citrullinemia
   12. Ornithine transcarboxylase deficiency
   13. Familial amyloid polyneuropathy (requires transplantation - polyneuropathy and cardiac amyloidosis development due to the production of a variant transthyretin molecule by the liver)
   14. Oxalosis (primary)

D. Acute Diseases:
   1. Fulminant hepatic failure

E. Mass Occupying Lesions:
   1. Polycystic disease of the liver (requiring transplantation due to the anatomic complications of a hugely enlarged liver)
   2. Hepatoblastoma confined to the liver
   3. Primary hepatocellular carcinoma confined to the liver
   4. Hemangioendothelioma
   5. Hilar cholangiocarcinoma (CCA) with a cross-sectional diameter 3 cm or less in conjunction with neoadjuvant chemoradiation therapy and the tumor is unresectable or there is underlying liver disease such that the individual is not a candidate for resection

F. Vascular disease:
   1. Budd-Chiari Syndrome

G. Other:
   1. Cryptogenic cirrhosis

Liver Retransplantation

Retransplantation in individuals with graft failure of an initial liver transplant, due to either technical reasons or hyperacute rejection is considered **medically necessary.**

Retransplantation in individuals due to either chronic rejection or recurrent disease is considered **medically necessary** when the individual meets general selection criteria as defined below.

Investigational and Not Medically Necessary:

Liver transplants in individuals with extrahepatic malignancy, including, but not limited to non-hilar extrahepatic cholangiocarcinoma, intrahepatic cholangiocarcinoma or hepatocellular carcinoma when either condition extends beyond the liver, are considered **investigational and not medically necessary.**

Liver transplants for all other conditions that do not lead to end-stage organ failure due to irreversible liver damage are considered **investigational and not medically necessary.**

Xenotransplantation is considered **investigational and not medically necessary.**

Bioartificial liver devices are considered **investigational and not medically necessary.**

Note: For multi-organ transplant requests, criteria must be met for each organ requested. In those situations, a member may present with concurrent medical conditions which would be considered an exclusion or a comorbidity that would preclude a successful outcome, but would be treated with the additional organ transplant. Such cases will be reviewed on an individual basis for coverage determination to assess the member's candidacy for transplantation.

General Individual Selection Criteria

In addition to having end stage liver disease, the member must not have a contraindication as defined by the American Society of Transplantation in Guidelines for the Referral and Management of Patients Eligible for Solid Organ Transplantation (2001) listed below.

Absolute Contraindications- for Transplant *Recipients* include, but are not limited to, the following:

A. Metastatic cancer
B. Ongoing or recurring infections that are not effectively treated
C. Serious cardiac or other ongoing insufficiencies that create an inability to tolerate transplant surgery
D. Serious conditions that are unlikely to be improved by transplantation as life expectancy can be finitely measured
E. Demonstrated patient noncompliance, which places the organ at risk by not adhering to medical recommendations
F. Potential complications from immunosuppressive medications are unacceptable to the patient
G. Acquired immune deficiency syndrome (AIDS) (diagnosis based on Centers for Disease Control and Prevention [CDC] definition of CD4 count, 200 cells/mm^3) unless the following are noted:
    1. CD4 count greater than 200 cells/mm^3 for greater than 6 months
    2. HIV-1 RNA undetectable
    3. On stable anti-retroviral therapy greater than 3 months
    4. No other complications from AIDS (for example, opportunistic infection, including aspergillus, tuberculosis, coccidioidomycosis, resistant fungal infections, Kaposi's sarcoma or other neoplasm)
    5. Meeting all other criteria for liver transplantation*

*Steinman, Theodore, et al. Guidelines for the Referral and Management of Patients Eligible for Solid Organ Transplantation. Transplantation. Vol. 71, 1189-1204, No. 9, May 15, 2001.

Rationale

Transplantation for progressive liver disease that will ultimately lead to a fatal outcome, or end-stage liver disease, is currently accepted as a practical and established medical therapy. In 2022 there were 11,256 candidates listed for liver transplantation in the United States, with 9236 (8667 deceased donor and 569 living donor) transplants performed in 2021. Technical and pharmaceutical advances have made liver transplantation available to individuals who might not have previously qualified, such as those diagnosed with hepatitis or hepatocellular carcinoma (HCC), also known as malignant hepatoma. The question is no longer whether to perform this complex surgery but how to identify the best candidates. The careful selection of candidates utilizing specific selection criteria has steadily improved the transplantation survival rates. Based on transplant registry data from United Network for Organ Sharing (UNOS) dated 2008-2015 1-year, 3-year and 5-year survival data is 89.1%, 80.0%, and 71.8%, respectively.

In 2020, 94.4% of liver transplant recipients were adults. Alcohol associated liver disease was the most common cause (35.2%) followed by nonalcoholic steatohepatitis (34.6%). HCC was the cause of liver disease in 12.6% and HCV was the cause in 6.7%. In the pediatric population biliary atresia was the leading indication for transplant (33.2%), then other/unknown diagnosis (21.6%), metabolic (17.3%), other cholestatic conditions (13.1%), acute liver failure (7.7%), and hepatoblastoma (7.1%) (Organ Procurement Transplant Network (OPTN)/Scientific Registry of Transplant Recipients (SRTR), 2020).

In 2014, the American Association for the Study of Liver Diseases (AASLD) and the American Society of Transplantation (AST) issued joint guidelines on evaluation of adults for liver transplantation. The guidelines recommend liver transplantation for severe acute or advanced chronic liver disease after all effective medical treatments have been attempted. The formal evaluation should confirm the irreversible nature of the liver disease and lack of effective alternative medical therapy (AASLD, 2014).

The guidelines also stated that liver transplant is indicated for the following conditions:

- Acute liver failure complications of cirrhosis
- Liver-based metabolic condition with systemic manifestations
    - α1-Antitrypsin deficiency
    - Familial amyloidosis
    - Glycogen storage disease
    - Hemochromatosis
    - Primary oxaluria
    - Wilson disease
- Systemic complications of chronic liver disease.

The guidelines also included 1A recommendations (strong recommendation with high-quality evidence) for a liver transplant (LT) for:

- Patients with HIV infection are candidates for LT if immune function is adequate and the virus is expected to be undetectable by the time of LT.
- Candidates with HCV [hepatitis C virus] have the same indications for LT as for other etiologies of cirrhosis.

According to the AASLD many factors may affect the outcome of solid organ transplantation. Prior to transplantation the facility should complete an assessment of the individuals medical and psychosocial status to confirm that transplantation is the best treatment option for managing the individuals disease and review of contraindications.

Potential Contraindications to Liver Transplant Include:

MELD [Model for End-stage Liver Disease] 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
Hemangiosarcoma
Persistent noncompliance
Lack of adequate social support system

The 2019 AASLD guideline on alcohol-associated liver disease provides recommendations on the timing of referral and selection of candidates for liver transplant. The guidance notes that the individual's history of alcohol addiction is a primary driver in selecting appropriate candidates for liver transplantation. Decompensated alcohol-associated cirrhosis (AAC), Child-Pugh-Turcotte class C cirrhosis, or a MELD-Na score ≥ 21 should trigger an evaluation and consideration for liver transplantation. The authors suggest that candidate selection, **"should not be based solely on a fixed interval of abstinence"**and instead a formal psychological evaluation can help stratify individuals into higher- or lesser-risk strata for relapse.

In 2023 the AASLD published updated practice guidance on the prevention, diagnosis, and treatment of hepatocellular carcinoma. The recommendations regarding liver transplant include:

> 7.b. All patients listed for liver transplantation should undergo semiannual HCC surveillance because identification of early-stage HCC changes priority for transplantation (Level 3, Strong Recommendation).
>
> 33.c. Liver transplantation should be the treatment of choice for transplant-eligible patients with HCC that recur within Milan criteria after surgical resection (Level 3, Strong Recommendation).
>
> 34. AASLD advises the use of pre-transplant locoregional bridging therapy for patients being evaluated or listed for liver transplantation, if they have adequate hepatic reserve, to reduce the risk of waitlist dropout in the context of anticipated prolonged wait times for transplant (Level 3 strong recommendation).

According to the American College of Gastroenterology (ACG) clinical guideline for alcoholic liver disease, liver transplantation may be considered for highly selected individuals with severe alcoholic hepatitis (AH) (strong recommendation, moderate level of evidence). The panel recommends that individuals be referred for liver transplant evaluation for alcoholic cirrhosis while formulating a plan for managing end-stage alcoholic liver disease. Individuals too sick to complete alcohol rehabilitation therapy may be considered for transplantation via an exception through the individual centers policy and complete the rehabilitation therapy after transplantation (Singal, 2018).

Puia and colleagues (2021) published a summary of eight ongoing trials studying liver transplantation for colorectal liver metastases using the Oslo score. The Oslo score evaluates the overall survival of liver transplant (LT) candidates, giving one point for each of the following prognostic factors present:

- Tumors larger than 5.5 cm
- CEA over 80 µg/L
- Surgery of the primary less than 2 years before the LT
- Progression of metastases at the time of LT

The authors concluded that although recent results of LT for nonresectable colorectal liver metastases are encouraging, current data are based mostly on small, single center, heterogeneous studies. More robust studies with well controlled methodologies are needed before including this option in the treatment of individuals with nonresectable colorectal liver metastases.

In 2023 the ACG published Acute Liver Failure (ALF) Guidelines which state that etiology is an essential indicator for prognosis and treatment, especially for the necessity for liver transplantation. Etiology is an independent predictor of waitlist mortality but not post-transplant outcomes. In individuals with ALF the ACG recommends using either the King's College criteria (KCC) or MELD score for liver transplant prognostication. Additionally, patients meeting the KCC criteria or presenting with MELD > 25 are at high risk of poor outcomes (conditional recommendation, strength of the recommendation is low)(Shingina, 2023).

Key concepts highlighted in the 2023 guidelines include etiology specific management regarding liver transplant:

> Mushroom poisoning: In patients presenting with mushroom poisoning and acute liver injury, Escudie criteria can be used to predict the need for liver transplantation even before the development of encephalopathy. Gastric lavage and activated charcoal should be administered within the first few hours after ingestion, provided no contraindications exist.
>
> Wilson disease: In patients presenting with ALF due to suspected or confirmed Wilson disease, liver transplantation evaluation should be initiated during diagnosis because of the lack of effective medical therapy.
>
> Autoimmune Hepatitis (AIH): In patients presenting with Acute Severe AIH, we suggest the use of IV corticosteroids. In patients with AS-AIH, which has progressed to ALF, we recommend early evaluation for liver transplantation.

The National Comprehensive Cancer Network (NCCN®) Clinical Practice Guidelines (CPG) (V2.2023) in Oncology™ for biliary tract cancers includes the following 2A recommendations regarding liver transplant for the treatment of extrahepatic cholangiocarcinoma (CCAs):

> Before biopsy, evaluate if patient is a resection or transplant candidate. If patient is a potential transplant candidate, consider referral to transplant center before biopsy. Unresectable perihilar or hilar cholangiocarcinomas that measure ≤3 cm in radial diameter, with the absence of intrahepatic or extrahepatic metastases and without nodal disease, as well as those with primary sclerosing cholangitis, may be considered

for liver transplantation at a transplant center that has an UNOS-approved protocol for transplantation of CCA. Surgery may be performed when index of suspicion is high; biopsy is not required.

There is retrospective evidence showing selected individuals with hilar CCA receiving preoperative chemoradiation therapy followed by liver transplantation have significantly improved overall survival compared with individuals undergoing resection. In 2022, the Liver and Intestinal Organ Transplantation OPTN committee updated the UNOS allocation of liver policy with MELD - exception criteria for liver transplant candidates with hilar CCA. Criteria includes standardized exception for candidates who have received neoadjuvant therapy prior to transplantation and present with cross-sectional imaging demonstrating a hilar mass measuring 3 cm or less in radial diameter.

The NCCN® CPG (V1.2023) in Oncology™ for hepatocellular carcinoma (HCC) provides a 2A recommendation for individuals meeting the "UNOS criteria ([AFP level ≤ 1000 ng/mL and single lesion ≥ 2 cm and ≤ 5cm, or 2 or 3 lesions ≥ 1 cm and ≤ 3cm,] should be considered for transplantation [cadaveric or living donation])."

Liver transplantation should be considered only for highly selected patients (i.e., tumor ≤ 3 cm in radial diameter, no intrahepatic or extrahepatic metastases, no nodal disease) with either unresectable disease with otherwise normal biliary and hepatic function or underlying chronic liver disease precluding surgery.

The NCCN also states there are individuals whose tumor characteristics are marginally outside of the UNOS guidelines who should be considered for transplant. Furthermore, there are individuals who are downstaged to within criteria that can also be considered for transplantation. Candidates are eligible for a standardized MELD exception before completing locoregional therapy per the NCCN recommendations.

In the recent NCCN CPG (V1.2023) in Oncology™ for neuroendocrine and adrenal tumors (NETs) the NCCN panel considers liver transplantation investigational for liver metastases of NETs of the gastrointestinal tract (well-differentiated grade 1/2). The panel acknowledges the considerable associated risk with liver transplantation, which is deemed to not be part of routine care at this time. The panel's recommendation is based on several series that reported results of liver transplantation in individuals with carcinoid tumors whose metastases were confined to the liver, as well as:

> Results from a multicenter database of 85 patients at 28 centers who underwent liver transplantation for NETs were also reported. A meta-analysis showed that, while 5-year survival rates are encouraging, the majority of patients undergoing liver transplantation ultimately develop recurrence. The panel acknowledged the considerable associated risks and deemed liver transplantation investigational and not part of routine care at this time.

Although the potential benefits are considerable, the use of xenotransplantation raises concerns regarding the potential infection of recipients with both recognized and unrecognized infectious agents and the possible subsequent transmission to their close contacts and into the general human population. A particular public health concern is the potential for cross-species infection by retroviruses, which may be latent and lead to disease years after infection. Moreover, new infectious agents may not be readily identifiable with current techniques. At the present time xenotransplantation is considered investigational and not medically necessary.

A bioartificial liver device is a device that uses living liver cells housed in extracorporeal (outside the body) cartridges to provide temporary liver function. For some medical conditions, the device would be used to keep individuals alive and healthier until a transplantable liver becomes available. At this time there is limited scientific evidence available to support the safety and efficacy of this device and therefore bioartificial liver devices are considered investigational and not medically necessary.

Background/Overview

A liver transplant consists of replacing an end-stage diseased liver with a healthy one. The liver is obtained from either a deceased or a living donor (a living donor gives only a segment of his/her liver to the recipient). In an orthotopic liver transplantation, the donor liver is placed in its correct anatomic location. A heterotopic liver transplantation refers to placement of the donor liver in a different location, typically with the native liver remaining in situ. The overwhelming majority of liver transplantations are orthotopic.

Split liver transplantation refers to dividing a donor liver into two grafts that can be used for two recipients. Generally, a pediatric recipient receives the left lobe and an adult recipient receives the right lobe.

Living-related donor transplantation of the left lateral segment primarily benefits children and is usually performed between parent and child. Adult-to-adult living donor transplantation uses the right lobe of the liver from a related or unrelated donor. Living donation allows the procedure to be scheduled electively, shortens the preservation time for the donor liver and allows time to optimize the recipient's condition pre-transplant.

The limiting factor for liver transplantation is the short supply of donor organs. At the time of this writing, the procurement and distribution of organs for transplantation in the United States is under the direction of the UNOS. In 1990, UNOS established an organ allocation system based on the principles of medical urgency and local priority. In 2002, UNOS replaced the original liver allocation system with a new scoring system based on objective laboratory data, referred to as MELD/PELD (Pediatric End-stage Liver Disease). MELD is a numerical scale, ranging from 6 (less ill) to 40 (gravely ill) that is used for adults, giving each individual a score (number) based on how urgently they need a liver transplantation in the next 3 months. The number is calculated by a formula using bilirubin, prothrombin time, and creatinine. PELD considers a child's bilirubin, prothrombin time, albumin, growth failure, and whether the child is less than 1 year old. In 2020 UNOS updated the transplant MELD or PELD exception extension policy; candidates can also receive additional points to increase their MELD/PELD score for conditions such as primary HCC, when tumors meet the modified Tumor-Node-Metastasis (TNM) staging classification. UNOS maintains a national database of transplant candidates, donors, recipients, donor-recipient matching, and histocompatibility (UNOS, 2022).

Xenotransplantation is any procedure that involves the transplantation, implantation, or infusion into a human recipient of either (a) live cells, tissues, or organs from a nonhuman animal source, or (b) human body fluids, cells, tissues, or organs that have had ex-vivo contact with live nonhuman animal cells, tissues, or organs. The development of xenotransplantation is, in part, driven by the fact that the demand for human organs for clinical transplantation far exceeds the supply.

Definitions

Cadaver: The physical remains of a deceased person.

End-stage: Being or occurring in the final stages of a terminal disease or condition.

Extrahepatic disease: Cancer that is located outside of the liver.

Fulminant liver failure: The onset of hepatic encephalopathy within 8 weeks of the first symptoms of liver disease.

Hepatoblastoma: A rare cancerous liver tumor occurring in infants and children that is composed of tissue resembling fetal or mature liver cells.

Heterotopic: Grafted or transplanted into an abnormal position.

In situ: In the natural or original position.

MELD: Model for End-Stage Liver Disease.

Orthotopic: Relating to the grafting of tissue in a natural position.

PELD: Pediatric end-stage liver disease.

Primary hepatocellular cancer: A cancer that originates within liver cells, as opposed to having spread to the liver from other organs.

Xenotransplantation: The surgical removal of an organ or tissue from an animal species and transplanting it into a human.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services may be Medically Necessary when criteria are met:

CPT	
00796	Anesthesia for intraperitoneal procedures in upper abdomen including laparoscopy; liver transplant (recipient)
47133	Donor hepatectomy, (including cold preservation), from cadaver donor
47135	Liver allotransplantation; orthotopic, partial or whole, from cadaver or living donor, any age
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, 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 2 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 2 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

ICD-10 Procedure	
0FT00ZZ	Resection of liver, open approach
0FT04ZZ	Resection of liver, percutaneous endoscopic approach
0FY00Z0	Transplantation of liver, allogeneic, open approach
0FY00Z1	Transplantation of liver, syngeneic, open approach

ICD-10 Diagnosis	
	All diagnoses

When services are Investigational and Not Medically Necessary:
For the procedure codes listed above when criteria are not met; or when the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

When services are also Investigational and Not Medically Necessary:

ICD-10 Procedure	
0FY00Z2	Transplantation of liver, zooplastic, open approach
5A1C00Z	Performance of biliary filtration, single
5A1C60Z	Performance of biliary filtration, multiple

ICD-10 Diagnosis	
	All diagnoses

References

Peer Reviewed Publications:

1. Abecassis M, Adams M, Adams P, et al. Consensus statement on the live organ donor. JAMA. 2000; 284(22):2919-2926.
2. Abouna GJM. Emergency adult to adult living donor liver transplantation for fulminant hepatic failure-is it justifiable? Transplantation. 2001; 71(10):1498-1500.

3. Allen JW, Hassanein T, Bhatia SN. Advances in bioartificial liver devices. Hepatology. 2001; 34(3):447-455.
4. Chamuleau RA. Bioartificial liver support. Metab Brain Dis. 2002; 17(4):485-491.
5. Ding YT, Qiu YD, Chen Z, et al. The development of a new bioartificial liver and its application in 12 acute liver failure patients. World J Gastroenterol. 2003; 9(4):829-832.
6. Dumortier J, Czyglik O, Poncet G, et al. Eversion thrombectomy for portal vein thrombosis during liver transplantation. Am J Transplant. 2002; 2(10):934-938.
7. Efrati O, Barak A, Modan-Moses D, et al. Liver cirrhosis and portal hypertension in cystic fibrosis. Eur J Gastroenterol Hepatol. 2003; 15(10):1073-1078.
8. Emre S, Kitibayashi K, Schwartz ME, et al. Liver transplantation in a patient with acute liver failure due to sickle cell intrahepatic cholestasis. Transplantation. 2000; 69(4):675-676.
9. Fridell JA, Bond GJ, Mazariegos GV, et al. Liver transplantation in children with cystic fibrosis: a long term longitudinal review of a single center's experience. J Pediatr Surg. 2003; 38(8):1152-1156.
10. Haberal M, Karakayali H, Emiroğlu R, et al. Living-donor split-liver transplantation. Transplant Proc. 2001; 33(5):2726-2729.
11. Heimbach JK. Evolution of liver transplantation selection criteria and U.S. allocation policy for patients with hepatocellular carcinoma. Semin Liver Dis. 2020; 40:358-364.
12. Heimbach JK, Haddock MG, Alberts SR, et al. Transplantation for hilar cholangiocarcinoma. Liver Transpl. 2004; 10(10 Suppl 2):S65-68.
13. Huang KW, Chao A, Chou NK, Ko WJ. Hepatic encephalopathy and cerebral blood flow improved by liver dialysis. Int J Artif Organs. 2003; 26(2):149-151.
14. Kim-Schluger L, Florman SS, Gondolesi G, et al. Liver transplantation at Mount Sinai. Clin Transpl. 2000; Chapter 21:247-253.
15. Lim KJ, Keeffe EB. Liver transplantation for alcoholic liver disease: current concepts and length of sobriety. Liver Transpl. 2004; 10(10 Suppl 2):S31-38.
16. Mazzaferro V. Results of liver transplantation: with or without Milan criteria? Liver Transpl. 2007; 13(11 Suppl 2):S44-47.
17. Michler RE. Xenotransplantation: risks, clinical potential and future prospects. Emerg Infect Dis. 1996; 2(1):64-70.
18. Molmenti EP, Roodhouse TW, Molmenti H, et al. Thrombendvenectomy for organized portal vein thrombosis at the time of liver transplantation. Ann Surg. 2002; 235(2):292-296.
19. Molmenti EP, Squires RH, Nagata D, et al. Liver transplantation for cholestasis associated with cystic fibrosis in the pediatric population. Pediatr Transplant. 2003; 7(2):93-97.
20. Moreno-Gonzalez E, Meneu-Diaz JC, Garcia G, et al. Simultaneous liver-kidney transplant for combined renal and hepatic end-stage disease. Transplant Proc. 2003; 35(5):1863-1865.
21. Nair S, Verma S, Thuluvath PJ. Obesity and its effect on survival in patients undergoing orthotopic liver transplantation in the United States. Hepatology. 2002; 3591):105-109.
22. Nishizaki T, Ikegami T, Hiroshige S, et al. Small graft for living donor liver transplantation. Ann Surg. 2001; 233(4):575-580.
23. Pomfret EA, Pomposelli JJ, Lewis WD, et al. Live donor adult liver transplantation using right lobe grafts: donor evaluation and surgical outcome. Arch Surg. 2001; 13694):425-433.
24. Puia-Negulescu S, Lebossé F, Mabrut JY, et al. Liver transplantation for colorectal liver metastases: current management and future perspectives. Int J Mol Sci. 2021; 22(6):3093.
25. Rea DJ, Heimbach JK, Rosen CB, et al. Liver transplantation with neoadjuvant chemoradiation is more effective than resection for hilar cholangiocarcinoma. Ann Surg. 2005; 242(3):451-458; discussion 458-461.
26. Sakamoto S, Uemoto S, Uryuhara K, et al. Graft size assessment and analysis of donors for living donor liver transplantation using right lobe. Transplantation. 2001; 71(10):1407-1413.
27. Sher LS, Levi DM, Wecsler JS, et al. Liver transplantation for metastatic neuroendocrine tumors: outcomes and prognostic variables. J Surg Oncol. 2015; 112(2):125-132.
28. Shingina A, Nizar M, Wakim-Fleming J et al. American Journal of Gastroenterology. Acute liver failure guidelines. Am J Gastroenterol. 2023; 118: 1128-1153. Epub: March 20, 2023. Available at: https://journals.lww.com/ajg/fulltext/2023/07000/acute_liver_failure_guidelines.14.aspx. Accessed on September 6, 2023.
29. Singal AK, Bataller R, Ahn J, et al. American Journal of Gastroenterology. Alcoholic liver disease. Am J Gastroenterol. 2018; 113(2): 175-194.
30. Smith CM, Davies DB, McBride MA. Liver transplantation in the United States: a report from the organ procurement and transplantation network. Clin Transpl. 2000; Chapter 2:19-30.
31. Steinman TI, Becker BN, Frost AE, et al. Guidelines for the referral and management of patients eligible for solid organ transplantation. Transplantation. 2001; 71(9):1189-1204.
32. Sugawara Y, Makuuchi M, Takayama T, et al. Small-for-size grafts in living-related liver transplantation. J Am Coll Surg. 2001; 192(4):510-513.

Government Agency, Medical Society, and Other Authoritative Publications:

1. American Association for the Study of Liver Disease (AASLD). Practice Guidelines. AASLD Guidelines for the treatment of hepatocellular carcinoma. 2018. Available at: https://www.aasld.org/sites/default/files/2022-06/HCC-Guideline-2018.pdf. Accessed on August 28, 2023.
2. American Association for the Study of Liver Diseases (AASLD). Practice Guidelines: Diagnosis and treatment of alcohol-associated liver diseases: 2019 practice guidance from the American association for the Study of Liver Diseases. Available at: https://aasldpubs.onlinelibrary.wiley.com/doi/full/10.1002/hep.30866. Accessed on August 28, 2023.
3. American Association for the Study of Liver Diseases (AASLD). Practice Guidelines: Evaluation for liver transplantation in adults: 2013 practice guideline by the American Association for the Study of Liver Disease and the American Society of Transplantation. October 2014. Available at: https://www.aasld.org/practice-guidelines/evaluation-adult-liver-transplant-patient. Accessed on August 28, 2023.
4. American Association for the Study of Liver Disease (AASLD). Practice Guidelines. 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. October 2014. Available at: https://www.aasld.org/practice-guidelines/evaluation-pediatric-liver-transplant-patient. Accessed on August 28, 2023.
5. American Association for the Study of Liver Disease (AASLD). Practice guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. 2023. Available at: https://journals.lww.com/hep/Citation/9900/AASLD_practice_guidance_on_prevention,_diagnosis,.441.aspx. Accessed on September 5, 2023.
6. American Society of Transplant Surgeons' position paper on adult-to-adult living donor liver transplantation. Liver Transplant 2000; 6(6):815-817.
7. Centers for Medicare and Medicaid Services. National Coverage Determination. Available at: http://www.cms.hhs.gov/mcd/index_chapter_list.asp. Accessed on August 28, 2023.
    - Adult Liver Transplantation. NCD #260.1. Effective June 21, 2012.
    - Pediatric Liver Transplantation. NCD #260.2. Effective April 21, 1991.

8. NCCN Clinical Practice Guidelines in Oncology™ (NCCN). © 2023 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website at: http://www.nccn.org/index.asp. Accessed on September 5, 2023.
    - Hepatocellular Carcinoma: Version 1.2023. March 10, 2023.
    - Biliary Tract Cancers: Version 2.2023. May 10, 2023.
    - Neuroendocrine and Adrenal Tumors (Version 1.2023). Updated August 2, 2023.
9. United Network for Organ Sharing (UNOS). Organ Procurement and Transplantation Network. Policies: 9: allocation of livers and liver-intestines. Revised September 6, 2022. Available at: http://optn.transplant.hrsa.gov/governance/policies/. Accessed on August 28, 2023.
10. U.S. Department of Health and Human Services. Scientific Registry of Transplant Recipients (SRTR). Updated 2022. Available on: https://srtr.transplant.hrsa.gov/annual_reports/Default.aspx. Accessed on August 28, 2023.

Websites for Additional Information

1. American Cancer Society. Available at: https://www.cancer.org. Accessed on August 28, 2023.
2. Centers for Disease Control and Prevention. Using viral load data to monitor HIV burden and treatment outcomes in the United States. February 2012. Available at: https://www.cdc.gov/hiv/pdf/library/factsheets/using-viral-load-data-monitor-hiv-burden-treatment-outcomes.pdf. Accessed on August 28, 2023.
3. National Cancer Institute. Available at: http://www.cancer.gov/cancertopics/types/alphalist. Accessed on August 28, 2023.
    - Adult primary liver cancer treatment Cancer (PDQ®): January 19, 2022.
4. National Institute of Diabetes and Digestive and Kidney Disease. Liver transplant. Last updated March 2017. Available at: https://www.niddk.nih.gov/health-information/liver-disease/liver-transplant. Accessed on. August 28, 2023.
5. United Network for Organ Sharing. Available at: http://www.unos.org. Accessed on August 28, 2023.

Index

Bioartificial Liver Device (BAL)
Liver Transplant: Orthotopic and Heterotopic
LIVERx 200™ Bioartificial Liver System
Sybiol® Synthetic Bio-Liver Device
Transplant, Liver
Xenotransplantation

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

Status	Date	Action
Reviewed	11/09/2023	Medical Policy & Technology Assessment Committee (MPTAC) review. Updated Rationale, References and Websites sections.
Reviewed	11/10/2022	MPTAC review. Updated Rationale, Background, References and Websites sections.
Reviewed	11/11/2021	MPTAC review. Updated Rationale, Background, References and Websites sections.
Reviewed	11/05/2020	MPTAC review. Updated Rationale, Background, References and Websites sections.
Reviewed	11/07/2019	MPTAC review. Updated Rationale, Background, References and Websites sections.
Reviewed	01/24/2019	MPTAC review. Updated Rationale, References and Websites sections.
Reviewed	03/22/2018	MPTAC review. The document header wording updated from “Current Effective Date” to “Publish Date.” Updated Rationale, Background, References and Websites sections.
Reviewed	05/04/2017	MPTAC review. Updated formatting in position statement section. Updated References and Websites sections.
Revised	05/05/2016	MPTAC review. Defined abbreviation in absolute contraindication section and corrected grammatically error in position statement. Updated Rationale, References and Websites sections.
	01/01/2016	Updated Coding section with 01/01/2016 CPT changes, removed 47136 deleted 12/31/2015; also removed ICD-9 codes.
Reviewed	05/07/2015	MPTAC review. Updated Description, Rationale, References and Websites.
Reviewed	05/15/2014	MPTAC review. Updated References and Websites.
Revised	05/09/2013	MPTAC review.
Revised	05/08/2013	Hematology/Oncology Subcommittee. Added medically necessary clinical indication for mass occupying lesion: hilar cholangiocarcinoma. Updated investigational and not medically necessary statement for extrahepatic malignancy to include non-hilar extrahepatic cholangiocarcinoma and intrahepatic cholangiocarcinoma. Updated Rationale, References and Websites.
Reviewed	11/08/2012	MPTAC review. Updated Background, References and Websites.
Reviewed	11/17/2011	MPTAC review. Updated References and Websites.
Revised	11/18/2010	MPTAC review. Updated medically necessary covered conditions for liver transplantation. Definitions, References and Websites updated.
Reviewed	11/19/2009	MPTAC review. Clarification of Investigational and Not Medically Necessary statement. Updated definitions and references.
Reviewed	11/20/2008	MPTAC review. Updated references.
Reviewed	11/29/2007	MPTAC review. Updated references. The phrase “investigational/not medically necessary” was clarified to read “investigational and not medically necessary.”
Reviewed	12/07/2006	MPTAC review. References updated. Coding updated; removed CPT 47134 deleted 12/31/03.
Revised	12/01/2005	MPTAC review. Addition of cryptogenic cirrhosis under the list of liver diseases leading to end organ liver failure. Clarification of investigational/not medically necessary statement.

	11/17/2005	Added reference for Centers for Medicare and Medicaid Services (CMS) – National Coverage Determination (NCD).
Revised	07/14/2005	MPTAC review.
Revised	04/28/2005	MPTAC review. Revision based on Pre-merger Anthem and Pre-merger WellPoint Harmonization.

Pre-merger Organizations	Last Review Date	Document Number	Title
Anthem, Inc.	09/18/2004	TRANS.00008	Liver Transplant
WellPoint Health Networks, Inc.	12/02/2004	7.06.02	Liver Transplantation

---

Applicable to Commercial HMO members in California: When a medical policy states a procedure or treatment is investigational, PMGs should not approve or deny the request. Instead, please fax the request to Anthem Blue Cross Grievance and Appeals at fax # 818-234-2767 or 818-234-3824. For questions, call G&A at 1-800-365-0609 and ask to speak with the Investigational Review Nurse.

Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The member's contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.