Clinical Policy: Pediatric Liver Transplant

Reference Number: LA.CP.MP.120 Coding Implications
Date of Last Revision: ~~34~~/23~~5/22~~ Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
End stage liver disease presents unique clinical considerations in the pediatric population. Liver transplantation provides a therapeutic option for pediatric patients with end stage disease. This policy establishes the medical necessity requirements for pediatric liver transplants.

Policy/Criteria

I. It is the policy of Louisiana Healthcare Connections that pediatric liver transplantation for pediatric members/enrollees (age < 18) with end stage liver disease is **medically necessary** when all of the following conditions are met:

a. End-stage liver disease has resulted in any of the following:
   1. Life expectancy ≤ 18 months without liver transplant;
   2. Unacceptable quality of life;
   3. Growth failure or reversible neurodevelopment impairment;

b. End-stage liver disease is due to one of the following:
   1. Cholestatic diseases, one of the following
      a. Biliary atresia, any of the following:
         i. Pre-hepatoportoenterostomy in infants with evidence of decompensated liver disease;
         ii. Post-hepatoportoenterostomy ~~beyond 3 months from procedure,~~ and any of the following:
            a) Total bilirubin > 6 mg/dL beyond three months from hepatoportoenterostomy;

~~ii.~~

            ~~a)~~b) Total bilirubin remains between 2 to 6 mg/dL;~~≥ 2;~~
            ~~b)~~c) Total bilirubin < 2 with unmanageable complications due to biliary cirrhosis or portal hypertension;
      b. Familial intrahepatic cholestasis 1 (FIC1) disease if partial external biliary diversion or ileal exclusion failed or could not be performed~~;~~
      c. Primary sclerosing cholangitis;
      d. Alagille Syndrome;
   2. Acute liver failure, all of the following:
      a. Absence of a known, chronic liver disease;
      b. Liver-based coagulopathy that is not responsive to parenteral vitamin K;
      c. International Normalized Ratio (INR), one of the following:
         i. Between 1.5 and 1.9 with clinical evidence of encephalopathy;
         ii. ≥ 2.0 regardless of the presence of clinical encephalopathy;
   3. Hepatocellular or vascular disease, any of the following:
      ~~a.~~ Autoimmune hepatitis with any of the following ~~with acute liver failure associated with encephalopathy\;~~
         i. Acute liver failure associated with encephalopathy;
         ii. Complications of end-stage liver disease not responsive to medical therapy;

~~a.~~

b. Decompensated liver disease, recurrent cholangitis, unmanageable bile duct strictures, or concerns for the risk of cholangiocarcinoma;

~~b.~~c. Budd-Chiari Syndrome

4. Malignancies, any of the following
   a. Hepatoblastoma, either of the following:
      i. Nonmetastatic and unresectable;
      ii. At the time of diagnosis or n~~N~~o later than after two~~2~~ rounds of chemotherapy;
   b. Hepatoblastoma with pulmonary metastases, any of the following:
      i. Chest CT is clear of metastases following chemotherapy;
      ii. A pulmonary wedge resection of the identified tumor reveals margins free of the tumor;
   c. Hepatocellular carcinoma with no evidence of extrahepatic disease;
   d. Infantile ~~H~~hemangioma~~endothelioma~~, any of the following:
      i. The hemangioendothelioma is not responding ~~Has failed~~ medical therapy;
      ii. The hemangioendothelioma is a~~A~~ssociated with life-threatening complications;
5. Metabolic or genetic disorders, any of the following:
   a. Alpha-1 antitrypsin deficiency;
   b. Wilson's disease;
   c. Severe urea cycle defects in the first year of life;
   d. Crigler-Najjar Type I at the time of diagnosis;
   e. Gestational alloimmune liver disease (previously known as neonatal hemochromatosis);
   f. Cystic fibrosis with unmanageable complications of portal hypertension;
   g. Multidrug resistance protein ~~-~~3 (MDR-3) disease that fails to respond to ursodeoxycholdic acid;

~~h.~~ Hereditary tyrosinemia type 1, any of the following; ~~that is not responsive to medical therapy~~;

h.

i. Progressive liver disease despite compliance with NTBC
ii. Rising AFP while on NTBC
iii. Change in liver imaging with a single nodule measuring > 10 mm or an increase in the number or size of hepatic nodules;
iv. Management with NTBC and diet cannot be adequately maintained

~~a.~~

~~a.~~i. Glycogen storage disease (GSD), ~~and~~ any of the following:
   i. GSD I, any of the following:
      a) Poor metabolic control;
      b) Multiple hepatic adenomas;
      c) Concern for hepatocellular carcinoma;
   ii. GSD III or GSD IV, any of the following:
      a) Poor metabolic control;
      b) Complications of cirrhosis;
      c) Progressive hepatic failure;

d) Suspected liver malignancy;

~~i.~~

~~ii. Glycogen storage disease (GSD), any of the following:~~

~~iii. GSD I, any of the following:~~

~~a)e) Poor metabolic control;~~

~~b)f) Multiple hepatic adenomas;~~

~~g) Concern for hepatocellular carcinoma;~~

j. Fatty acid oxidation defects, any of the following:

~~c)~~

~~iv. GSD III or GSD IV, any of the following:~~

~~a) Poor metabolic control;~~

~~b) Complications of cirrhosis;~~

~~c) Progressive hepatic failure;~~

~~d) Suspected liver malignancy;~~

~~iii. Fatty acid oxidation defects, any of the following:~~

~~v.~~i. Failed medical therapy;

ii. Experience recurrent episodes of complications;

k. Primary hyperoxaluria type 1 at the time of diagnosis

l. Organic acidemia, any of the following

i. Metabolic decompensation despite conventional therapy;

ii. Uncontrollable hyperammonemia;

iii. Restricted growth;

iv. Severe impairment of health-related quality of life, despite conventional therapy;

m. Inborn errors of bile acid synthesis or those refractory to medical therapy;

~~vi.~~

~~Inborn errors of bile acid synthesis or those refractory to medical therapy;~~

6. Fibrotic or cirrhotic conditions, any of the following:

a. Ductal plate malformations with recurrent cholangitis or complications of portal hypertension;

b. Parenteral nutrition-associated liver disease with enteral autonomy and complications of cirrhosis;

7. Miscellaneous conditions, any of the following:

a. Non-cirrhotic portal hypertension with cardiopulmonary complications;

b. Factor VII deficiency with complications from or failure of medical management;

c. Protein C deficiency, any of the following:

i. Failed medical therapy;

ii. Experiencing complications;

d. Hepatopulmonary syndrome (HPS) and any of the following:

i. Portosystemic shunting resulting from either a congenital or acquired vascular anomaly or liver disease (cirrhotic or noncirrhotic);

ii. Portal hypertension who are not candidates for closure of the shunt;

C. Does not have any of the following contraindications:

~~Primary hyperoxaluria type 1 at the time of diagnosis;~~

~~iv. Organic acidemia, any of the following:~~
~~vii. Metabolic decompensation despite conventional therapy;~~
~~viii. Uncontrollable hyper-ammonia;~~
~~ix. Restricted growth;~~
~~x. Severe impairment of health-related qualify of life, despite conventional therapy;~~
~~v. Inborn errors of bile acid synthesis or those refractory to medical therapy;~~
~~6. Fibrotic or cirrhotic conditions~~
~~a. Ductal plate malformations with recurrent cholangitis or complications of portal hypertension;~~
~~b. Parenteral nutrition-associated liver disease with enteral autonomy and complications of cirrhosis;~~
~~7. Miscellaneous conditions~~
~~a. Non-cirrhotic portal hypertension with cardiopulmonary complications;~~
~~b. Factor VIII deficiency that has failed medical therapy;~~
~~c. Protein C deficiency that has failed medical therapy;~~
~~d. Budd-Chiari Syndrome;~~
~~e. Does not have any of the following contraindications:~~

1. ~~Chronic~~ Active infection with highly virulent and/or resistant microbes that are poorly controlled pre-transplant;
2. HIV infection with detectable viral load;
3. Malignancy with high risk of recurrence or death related to cancer; (excluding malignancies that transplant could sufficiently address, as noted in I.B.4);
~~3.~~
4. Glomerular filtration rate < 40 mL/min/1.73m^2 unless being considered for multi-organ transplant;
5. Stroke, acute coronary syndrome, or myocardial infarction (excluding demand ischemia) within 30 days;
6. Severe, life threatening extrahepatic multi-organ mitochondrial disease;
7. Alper~~'~~s syndrome;
8. Valproate-associated liver failure ~~in a child under 10 years of age;~~
9. Severe portopulmonary hypertension that is not responsive to medical therapy;
10. Niemann-Pick disease type C;
11. Hemophagocytic lymphohistiocytosis presenting acute liver failure;
12. Acute renal failure with rising creatinine or on dialysis and low likelihood of recovery;
13. Septic shock;
14. Progressive cognitive impairment;
15. Other severe uncontrolled medical condition expected to limit survival after transplant;
16. Inability to adhere to the regimen necessary to preserve the transplant, even with caregiver support;
17. Absence of an adequate or reliable social support system;
18. Active substance use or dependence including current tobacco use, vaping, marijuana use~~smoking~~, (unless prescribed by a licensed practitioner), or IV drug use without convincing evidence of risk reduction behaviors, (unless urgent transplant timelines are present, in which case a commitment to reducing behaviors is acceptable) ~~such as~~

meaningful and/or long-term participation in therapy for substance abuse and/or dependence. Serial blood and urine testing may be used to verify abstinence from substances that are of concern.

Background

Liver transplantation is an effective therapeutic option for an assortment of acute and chronic hepatic disorders that lead to end stage liver disease in the pediatric population. According to the practice guideline of the American Association for the Study of Liver Diseases (AASLD), pediatric liver transplants account for ~7.8% of all liver transplants in the United States. [1]1 The evaluation of children for liver transplants should include a multidisciplinary team of specialists that achieve psychosocial, neurocognitive, and developmental needs as well as the complex clinical necessities of these patients.

For adult liver transplants (and children ≥ 12 years of age), the Model for Endstage Liver Disease (MELD) formula is commonly utilized to determine assess organ allocation for liver candidates. The Pediatric Endstage Liver Disease (PELD) score was analogously developed for children < 12 years of age and utilizes total serum bilirubin, INR, height, weight, and albumin; however, this scoring system is not ubiquitously utilized. [1]1

Common indications for pediatric liver transplants are acute liver failure, biliary atresia and other cholestatic diseases, metabolic diseases, immune disorders, and hepatic malignancies. A recent multicenter analysis of five-year survival of 461 children revealed an 88% survival rate for the first year. [5]5 The majority of these children also show strong graft function at five years, but there are multiple chronic post-transplantation complications in extrahepatic organs. [5]5

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Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2020, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only and may not support medical necessity. Inclusion or exclusion of any codes does not guarantee coverage ~~and may not support medical necessity~~. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

CPT® Codes	Description
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 and IV)
47142	Donor hepatectomy (including cold preservation), from living donor; total right lobectomy (segments V, VI, VII and VIII)
*47143	Backbench standard preparation of cadaver donor whole liver graft prior to allotransplantation, including cholecystectomy, if necessary, and dissection and removal of surrounding soft tissues to prepare the vena cava, portal vein, hepatic artery, and common bile duct for implantation; without trisegment or lobe split
*47144	Backbench standard preparation of cadaver donor whole liver graft prior to allotransplantation, including cholecystectomy, if necessary, and dissection and removal of surrounding soft tissues to prepare the vena cava, portal vein, hepatic artery, and common bile duct for implantation; with trisegment split of whole liver graft into 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

* All non-covered codes are reviewed for medical necessity for members under 21 years old

HCPCS Codes [SS1]	Description
S2152	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 posttransplant care in the global definition

ICD-10-CM Diagnosis Codes that Support Coverage Criteria

ICD-10-CM Code	Description
C22.0-C22.9	Malignant neoplasm of liver and intrahepatic bile ducts
D18.03	Hemangioma of intra-abdominal structures
D49.0	Neoplasm of unspecified behavior of digestive system
D68.59	Other primary thrombophilia
E70.21	Tyrosinemia
E70.29	Other disorders of tyrosine metabolism
E71.310-E71.318	Disorders of fatty-acid oxidation
E72.20-E72.29	Disorders of urea cycle metabolism
E72.53	Primary hyperoxaluria
E74.01	von Gierke disease
E74.03	Cori disease
E74.09	Other glycogen storage disease
E80.5	Crigler-Najjar syndrome
E83.01	Wilson's disease
E84.8	Cystic fibrosis with other manifestations
E88.01	Alpha-1-antitrypsin deficiency
E88.89	Other specified metabolic disorders
I82.0	Budd-Chiari syndrome
K71.0-K71.9	Toxic liver disease
K72.00-K72.91	Hepatic failure, not elsewhere specified
K74.00-K74.69	Fibrosis and cirrhosis of liver
K75.4	Autoimmune hepatitis
K76.6	Portal hypertension
K83.01-K83.09	Cholangitis
K83.1	Obstruction of bile duct
P19.0-P19.9	Metabolic academia in newborn
P78.84	Gestational alloimmune liver disease
Q44.0-Q44.7	Congenital malformations of gallbladder, bile ducts and liver

Reviews, Revisions, and Approvals	Reviewsion Date	Approval Date
Converted corporate to local policy.	02/2021	02/2021
Replaced contraindications regarding psychological condition preventing compliance with medical therapy and "current non-adherence to medical therapy" with "Inability to adhere to the regimen necessary to preserve the transplant, even with caregiver support." Changed "Review Date" in header to "Date of Last Revision," and "Date" in the revision log header to "Revision Date."	2/22	2/22
Edited contraindications: Replaced "non-hepatic malignancy…" with malignancy with high risk of recurrence or death…"; added GFR restriction, added HIV infection with detectable viral load, added stroke, acute coronary syndrome, or MI; added acute renal failure…; added septic shock; added progressive cognitive impairment; replaced "untreatable significant dysfunction of another major organ system…" with "Other severe uncontrolled medical condition expected to limit survival after transplant;" slightly reworded substance use contraindication. Added "and may not support medical necessity" to Coding Implications section	5/22	8/13/22
Annual review. Criteria I.B.1.a.ii. updated to remove "beyond 3 months from procedure" and added a) Total bilirubin > 6 mg/dL beyond three months from hepatoportoenterostomy b) Total bilirubin remains between 2 to 6 mg/dL. Updated Criteria I.B.1.b. to add "if partial external biliary diversion or ileal exclusion failed or could not be performed." Removed "acute liver failure associated with encephalopathy" in Criteria I.B.3.a. and added I.B.3.a.i. and ii. Added Criteria I.B.3.c. Budd-Chiari Syndrome. Added, "At the time of diagnosis…" to I.B.4.a.ii. Updated Criteria I.B.4.d. to infantile hemangioma as well as verbiage in I.B.4.d.i. and ii. Removed "that is not responsive to medical therapy" in criteria I.B.5.h. and added I.B.5.h.i. through iv. Criteria I.B.5.m.ii. changed from "hyper-ammonia" to "hyperammonemia." Criteria I.B.7.b. updated to Factor VII and updated to state, "with complications from or failure of medical management." Removed "that has failed medical therapy" from Criteria I.B.7.c. and added sub criteria i. and ii. Removed "Budd-Chiari Syndrome" from I.B.7.d. Added Hepatopulmonary syndrome (HPS) as I.B.7.d. and added sub criteria i. and ii. Criteria I.C.1. updated from "chronic" to "active" infection. Criteria I.C.3. updated and added note for exclusion of malignancies that transplant could sufficiently address. Criteria I.C.8. updated to remove age requirement. Criteria I.C.18. updated to exclude marijuana use when prescribed by a licensed practitioner and include required commitment to reducing substance use behaviors if urgent transplant timelines are present. Background updated with no impact on criteria. ICD-10	34/23	

Reviews, Revisions, and Approvals	Reviewsion Date	Approval Date
codes removed. References reviewed and updated. Reviewed by internal specialist and external specialist.		

References

1. Squires RH, Ng V, Romero R, et al. 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. *Hepatology*. 2014;60(1):362 to 398. doi:10.1002/hep.27191
2. Squires JE. Acute liver failure in children: Management, complications, and outcomes. UpToDate. www.uptodate.com. Published April 21, 2022. Accessed January 23, 2023.
3. Leonis MA, Balistreri WF. Evaluation and management of end-stage liver disease in children. *Gastroenterology*. 2008;134(6):1741 to 1751. doi:10.1053/j.gastro.2008.02.029
4. Ng VL, Fecteau A, Shepherd R, et al. Outcomes of 5-year survivors of pediatric liver transplantation: report on 461 children from a North American multicenter registry. *Pediatrics*. 2008;122(6):e1128 to e1135. doi:10.1542/peds.2008-1363
5. McKiernan P. Acute liver failure after valproate exposure: Liver transplantation may be indicated beyond childhood. *Liver Transpl*. 2014;20(11):1287 to 1289. doi:10.1002/lt.23988

1. Squires RH, Ng V, Romero R, et al. 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. *Hepatology*. 2014;60(1):362-398. doi:10.1002/hep.27191
2. Squires, R. H. Acute liver failure in children: Management, complications, and outcomes. UpToDate. www.uptodate.com. Published November 17, 2020. Accessed December 15, 2021.
3. Leonis MA, Balistreri WF. Evaluation and management of end-stage liver disease in children. *Gastroenterology*. 2008;134(6):1741-1751. doi:10.1053/j.gastro.2008.02.029
4. Ng VL, Fecteau A, Shepherd R, et al. Outcomes of 5-year survivors of pediatric liver transplantation: report on 461 children from a north american multicenter
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Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program

approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

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