Clinical Policy: Pediatric Liver Transplant

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 health plans affiliated with Centene Corporation® 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
         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 ≥ 2;
               b) Total bilirubin < 2 with unmanageable complications due to biliary cirrhosis or portal hypertension;
         b. Familial intrahepatic cholestasis;
         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
         a. Autoimmune hepatitis with acute liver failure associated with encephalopathy;
         b. Decompensated liver disease, recurrent cholangitis, unmanageable bile duct strictures, or concerns for the risk of cholangiocarcinoma;
      4. Malignancies, any of the following
         a. Hepatoblastoma, either of the following:
            i. Nonmetastatic and unresectable;
            ii. No later than after 2 rounds of chemotherapy;

See Important Reminder at the end of this policy for important regulatory and legal information.
Clinical Policy
Pediatric Liver Transplant

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. Hemangioendothelioma, any of the following:
      i. Has failed medical therapy;
      ii. Associated with life-threatening complications;

5. Metabolic or genetic disorders
   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. Neonatal hemochromatosis;
   f. Cystic fibrosis with unmanageable complications of portal hypertension;
   g. Multidrug resistance protein 3 disease that fails to respond to ursodeoxycholdic acid;
   h. Hereditary tyrosinemia type 1 that is not responsive to medical therapy;
   i. Glycogen storage disease (GSD), 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;
   j. Fatty acid oxidation defects, any of the following:
      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 hyper-ammonia;
      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;

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;
**CLINICAL POLICY**

**Pediatric Liver Transplant**

b. Factor VIII deficiency that has failed medical therapy;
c. Protein C deficiency that has failed medical therapy;
d. Budd-Chiari Syndrome;

C. Does not have any of the following contraindications:
1. Chronic infection with highly virulent and/or resistant microbes that are poorly controlled pre-transplant;
2. Non-hepatic malignancy, except for non-melanoma localized skin cancer that has been treated appropriately, a malignancy that has been completely resected, or a treated malignancy determined to have a small likelihood of recurrence and acceptable future risks;
3. Severe, life threatening extrahepatic multi-organ mitochondrial disease;
4. Alper’s syndrome;
5. Valproate-associated liver failure in a child under 10 years of age;
6. Severe portopulmonary hypertension that is not responsive to medical therapy;
7. Niemann-Pick disease type C;
8. Hemophagocytic lymphohistiocytosis presenting acute liver failure;
9. Current non-adherence to medical therapy or a history of repeated or prolonged episodes of non-adherence to medical therapy that are perceived to increase the risk of non-adherence after transplantation;
10. Psychiatric or psychological condition associated with the inability to cooperate or comply with medical therapy;
11. Untreatable significant dysfunction of another major organ system, unless combined organ transplantation can be performed;
12. Absence of an adequate or reliable social support system.
13. Substance abuse or dependence (including tobacco and alcohol) without convincing evidence of risk reduction behaviors, 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 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

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 5 year survival of 461 children revealed the first year survival rate to be 88%. The majority of these children also show strong graft function at 5 years, but there are multiple chronic post-transplantation complications in extrahepatic organs.

**Coding Implications**

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<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>
</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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### HCPCS Codes

<table>
<thead>
<tr>
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<tbody>
<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 posttransplant care in the global definition</td>
</tr>
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### ICD-10-CM Diagnosis Codes that Support Coverage Criteria

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

<table>
<thead>
<tr>
<th>ICD-10-CM Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>Q44.0-Q44.7</td>
<td>Congenital malformations of gallbladder, bile ducts and liver</td>
</tr>
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<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>Approval Date</th>
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<tbody>
<tr>
<td>Policy developed</td>
<td>02/18</td>
<td>04/18</td>
</tr>
<tr>
<td>Under fatty acid oxidation defects, changed recurrent episodes to “recurrent episodes of complications.” Other minor wording changes for clarity</td>
<td>12/18</td>
<td></td>
</tr>
<tr>
<td>Added to the valproate-associated liver failure contraindication that it applies to children under 10. Specialist reviewed. References reviewed and updated.</td>
<td>02/19</td>
<td>02/19</td>
</tr>
<tr>
<td>Added contraindication of substance use or dependence. Removed duplicative codes K72.01, K72.90 and K72.9. Updated K83.0 to K83.01-K83.09</td>
<td>01/20</td>
<td>01/20</td>
</tr>
<tr>
<td>Edited malignancy contraindication adding exceptions: cancer that has been completely resected, or that has been treated and poses acceptable future risk.</td>
<td>05/20</td>
<td>05/20</td>
</tr>
<tr>
<td>10/1/20 ICD-10 code update: replaced code range K74.0-K74.69 with K74.00- K74.69 to include new codes included in this range. Replaced “member” with “member/enrollee” in all instances</td>
<td>10/20</td>
<td></td>
</tr>
</tbody>
</table>

References

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. The Health Plan 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. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members/enrollees. This clinical policy is not intended to recommend treatment for members/enrollees. Members/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

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**Note:** For Medicaid members/enrollees, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

**Note:** For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable
Pediatric Liver Transplant

NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.

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