Corporate Medical Policy

Liver Transplant

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Origination:	12/1995
Last CAP Review:	5/2017
Next CAP Review:	5/2018
Last Review:	5/2017

Description of Procedure or Service

Liver transplantation is now routinely performed as a treatment of last resort for patients with end-stage liver disease. Liver transplantation may be performed with liver donation after brain or cardiac death or with a liver segment donation from a living donor. Patients are prioritized for transplant by mortality risk and severity of illness criteria developed by the Organ Procurement and Transplantation Network (OPTN) and the United Network of Organ Sharing (UNOS). The severity of illness is determined by the model for end-stage liver disease (MELD) and pediatric end-stage liver disease (PELD) scores.

The original liver allocation system was based on assignment to Status 1, 2A, 2B, or 3. Status 2A, 2B, and 3 were based on the Child-Turcotte-Pugh score, which included a subjective assessment of symptoms as part of the scoring system. In February 2002, Status 2A, 2B, and 3 were replaced with 2 disease severity scales: the model for end-stage liver disease (MELD) and pediatric end-stage liver disease (PELD) for patients younger than age 12 years scoring systems. In June 2013, OPTN/UNOS published its most recent allocation system, which previously expanded Status 1 to Status 1A and 1B in September 2012. Status 1A patients have acute liver failure with a life expectancy of less than 7 days without a liver transplant. Status 1A patients also include primary graft non-function, hepatic artery thrombosis and acute Wilson's disease. Status 1A patients must be recertified as Status 1A every 7 days. Status 1B patients are pediatric patients (ages 0-17 years) with chronic liver disease listed as: fulminant liver failure, primary nonfunction, hepatic artery thrombosis, acute decompensated Wilson's disease, chronic liver disease, and nonmetastatic hepatoblastoma. Pediatric patients move to Status 1A upon age18 but still qualify for pediatric indications.

Following Status 1, donor livers will be prioritized to those with the highest scores on MELD or PELD. With this allocation system, the highest priority for liver transplantation is given to patients receiving the highest number of points. MELD and PELD are a continuous disease severity scale based entirely on objective laboratory values. These scales have been found to be highly predictive of the risk of dying from liver disease for patients waiting on the transplant list. The MELD score incorporates bilirubin, prothrombin time (i.e., international normalized ratio [INR]), and creatinine into an equation, producing a number that ranges from 6 to 40. The PELD score incorporates albumin, bilirubin, INR, growth failure, and age at listing. Waiting time will only be used to break ties among patients with the same MELD or PELD score and blood type compatibility.

In the previous system, waiting time was often a key determinant of liver allocation, and yet waiting time was found to be a poor predictor of the urgency of liver transplant, since some patients were listed early in the course of their disease, while others were listed only when they became sicker. In the revised allocation systems, patients with a higher mortality risk and higher MELD/PELD scores will always be considered before those with lower scores, even if some patients with lower scores have waited longer. Status 7 describes patients who are temporarily inactive on the transplant waiting list due to being temporarily unsuitable for transplantation. Pediatric patients who turn 18 are Status X.

Due to the scarcity of donor livers, a variety of strategies have been developed to expand the donor pool. For example, split graft refers to dividing a donor liver into 2 segments that can be used for 2 recipients. Living donor liver transplantation (LDLT) is now commonly performed for adults and children from a related or unrelated donor. Depending on the graft size needed for the recipient, either the right lobe, left lobe or the left lateral segment can be used for LDLT. In addition to addressing the problem of donor organ scarcity, LDLT allows the procedure to be scheduled electively before the recipient's condition deteriorates or serious complications develop. LDLT shortens the preservation time for the donor liver and decreases disease transmission from donor to recipient.

Related Policies:

- Small Bowel, Small Bowel with Liver, or Multivisceral Transplant

Note:

Management of acute rejection of liver transplant using intravenous immunoglobulin (IVIG) is discussed separately in Policy Immunoglobulin Therapy. In addition, the role of chemoembolization in patients with hepatocellular cancer is addressed in the separate policy Chemoembolization of the Hepatic Artery, Transcatheter Approach.

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

BCBSNC will provide coverage for Liver Transplant when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

Benefits Application

Please refer to certificate for availability of benefit. Certificates may specifically exclude transplantation procedures from coverage. Certificate language should verify application of medical necessity in making benefit determinations. This policy relates only to the services or supplies described herein. Benefits may vary according to benefit design, therefore certificate language should be reviewed before applying the terms of the policy.

- Coverage for medically necessary liver transplant procedures will be determined based on the member's certificate, the medical criteria and guidelines for coverage, and review on an individual consideration basis.
- The benefit begins at the time of admission for the transplant, or once the patient is determined eligible for the transplant, which may include tests or office visits prior to the actual transplant.
- The benefit ends at the time of discharge from the hospital, or at the end of the required follow-up, including the immunosuppressive drugs administered on an outpatient basis.
- Expenses incurred in the evaluation and procurement of organs and tissues are benefits when billed by the hospital. Included in these expenses may be specific charges for participation with registries for organ procurement, operating rooms, supplies, use of hospital equipment, and transportation of the tissue or organ to be evaluated.

Additional services may be covered within the scope of the human organ transplant (HOT) benefit:

- Hospitalization of the recipient for medically recognized transplants from a donor to the transplant recipient
- Pre-hospital work-up and hospitalization of a living donor undergoing a partial hepatectomy (removal of part of the liver) should be considered as part of the recipient transplant costs

- Evaluation tests requiring hospitalization to determine the suitability of both potential and actual donors, when such tests cannot be safely and effectively performed on an outpatient basis
- Hospital, room, board, and general nursing in semi-private rooms
- Special care units, such as coronary and intensive care
- Hospital ancillary services
- Physicians' services for surgery, technical assistance, administration of anesthetics, and medical care
- Acquisition, preparation, transportation and storage of the organ
- Diagnostic services
- Drugs that require a prescription by federal law

Benefits are not generally available for the following:

1) Human organ transplant (HOT) services, for which the cost is covered/funded by governmental, foundation, or charitable grants.
2) Organs that are sold rather than donated to a recipient.
3) An artificial organ.

Certificates may specifically exclude certain transplant services (e.g., artificial organs). Please refer to certificate for "Transplants Exclusions".

When Liver Transplants are covered

A.) A liver transplant using a cadaver or living donor is considered medically necessary for carefully selected patients with end-stage liver failure due to irreversibly damaged livers from conditions that include, but are not limited to the following:

1) Hepatocellular diseases
    a) Alcoholic liver disease
    b) Viral hepatitis (A, B, C, or non-A, non-B)
    c) Autoimmune hepatitis
    d) Alpha-1 Antitrypsin deficiency
    e) Hemochromatosis
    f) Non-alcoholic steatohepatitis
    g) Protoporphyria
    h) Wilson's disease
2) Cholestatic liver diseases
    a) Primary biliary cirrhosis
    b) Primary sclerosing cholangitis with development of secondary biliary cirrhosis
    c) Biliary atresia
3) Vascular diseases
    a) Budd-Chiari syndrome
4) Primary hepatocellular carcinoma

5) Inborn errors of metabolism
6) Trauma and toxic reactions
7) Miscellaneous
    a) Familial amyloid polyneuropathy

Liver transplantation may be considered medically necessary in patients with polycystic disease of the liver who have massive hepatomegaly causing obstruction or functional impairment.

Liver transplantation may be considered medically necessary in patients with unresectable hilar cholangiocarcinoma.

Liver transplantation may be considered medically necessary in pediatric patients with nonmetastatic hepatoblastoma.

Liver *retransplantation* may be considered medically necessary in patients with:

a) Primary graft non-function
b) Hepatic artery thrombosis
c) Chronic rejection
d) Ischemic type biliary lesions after donation after cardiac death
e) Recurrent non-neoplastic disease causing late graft failure

When Liver Transplants are not covered

A) Liver transplantation is considered investigational in the following patients:

1) Patients with intrahepatic cholangiocarcinoma
2) Patients with neuroendocrine tumors metastatic to the liver

B) Liver transplantation is considered not medically necessary in the following patients:

1) Patients with hepatocellular carcinoma that has extended beyond the liver.
2) Patients with ongoing alcohol and/or drug abuse. (Evidence for abstinence may vary among liver transplant programs, but generally a minimum of 3 months is required.)

C) Liver Transplantation is considered investigational in all other situations not described above.

Policy Guidelines

It is recommended that all transplant requests be reviewed by the Plan Medical Director or his or her designee. Only those patients accepted for transplantation by a transplantation center and actively listed for transplant should be considered for precertification or prior approval. Guidelines should be followed for transplant network or consortiums, if applicable.

General

Potential contraindications subject to the judgment of the transplant center:

1. Known current malignancy, including metastatic cancer
2. Recent malignancy with high risk of recurrence
3. Untreated systemic infection making immunosuppression unsafe, including chronic infection
4. Other irreversible end-stage disease not attributed to liver disease
5. History of cancer with a moderate risk of recurrence
6. Systemic disease that could be exacerbated by immunosuppression
7. Psychosocial conditions or chemical dependency affecting ability to adhere to therapy

Liver Specific Patient Selection Criteria

The MELD and PELD scores range from 6 (less ill) to 40 (gravely ill). The MELD and PELD scores will change during the course of a patient's tenure on the waiting list.

Patients with liver disease related to alcohol or drug abuse must be actively involved in a substance abuse treatment program.

Patients with polycystic disease of the liver do not develop liver failure but may require transplantation due to the anatomic complications of a hugely enlarged liver. The MELD/PELD score may not apply to these cases. One of the following complications should be present:

- Enlargement of liver impinging on respiratory function
- Extremely painful enlargement of liver
- Enlargement of liver significantly compressing and interfering with function of other abdominal organs

Patients with familial amyloid polyneuropathy do not experience liver disease, per se, but develop polyneuropathy and cardiac amyloidosis due to the production of a variant transthyretin molecule by the liver. MELD/PELD exception criteria and scores may apply to these cases. Candidacy for liver transplant is an individual consideration based on the morbidity of the polyneuropathy. Many patients may not be candidates for liver transplant alone due to coexisting cardiac disease.

Criteria used for patient selection of hepatocellular carcinoma patients eligible for liver transplant include the Milan criteria, which is considered the criterion standard, the University of California, San Francisco (UCSF) expanded criteria, and UNOS criteria.

Milan criteria: a single tumor 5 cm or less in diameter or 2 to 3 tumors 3 cm or less

UCSF expanded criteria: a single tumor 6.5 cm or less or up to 3 tumors 4.5 cm or less, and a total tumor size of 8 cm or less

UNOS T2 criteria: a single tumor 1 cm or greater and up to 5 cm or less in diameter or 2 to 3 tumors 1 cm or greater and up to 3 cm or less and without extrahepatic spread or macrovascular invasion. UNOS criteria, which were updated in 2013, may prioritize T2 HCC that meet specified staging and imaging criteria by allocating additional points equivalent to a MELD score predicting a 15% probability of death within 3 months.

Patients with hepatocellular carcinoma are appropriate candidates for liver transplant only if the disease remains confined to the liver. Therefore, the patient should be periodically monitored while on the waiting list, and if metastatic disease develops, the patient should be removed from the transplant waiting list. In addition, at the time of transplant, a backup candidate should be scheduled. If locally extensive or metastatic cancer is discovered at the time of exploration prior to hepatectomy, the transplant should be aborted, and the backup candidate scheduled for transplant.

Note that liver transplantation for those with T3 HCC is not prohibited by UNOS guidelines, but these patients do not receive any priority on the waiting list. All patients with HCC awaiting transplantation are reassessed at 3-month intervals. Those whose tumors have progressed and are no longer T2 tumors will lose the additional allocation points.

Additionally, nodules identified through imaging of cirrhotic livers are given a Class 5 designation. Class 5B and 5T nodules are eligible for automatic priority. Class 5B criteria consist of a single nodule 2 cm or larger and up to 5 cm (T2 stage) that meets specified imaging criteria. Class 5T nodules have undergone subsequent loco-regional treatment after being automatically approved on initial application or extension. A single Class 5A nodule (greater than 1 cm and less than 2 cm) corresponds to T1 HCC and does not qualify for automatic priority. However, combinations of Class 5A nodules are eligible for automatic priority if they meet stage T2 criteria. Class 5X lesions are outside of stage T2 and are not eligible for automatic exception points. Nodules less than 1 cm are

considered indeterminate and are not considered for additional priority. Therefore, the UNOS allocation system provides strong incentives to use loco-regional therapies to downsize tumors to T2 status and to prevent progression while on the waiting list.

Summary

Liver transplant is an accepted treatment of end-stage liver disease that provides a survival benefit in appropriately selected patients and thus may be considered medically necessary for the above indications listed in the Policy Statement and in those otherwise meeting UNOS criteria. Liver transplantation is investigational in patients in whom the procedure is expected to be futile due to comorbid disease or in whom post-transplantation care is expected to significantly worsen comorbid conditions. Case series and case-control data indicate that human immunodeficiency virus (HIV)-infection is not an absolute contraindication to liver transplant; for patients who meet selection criteria, these studies have demonstrated patient and graft survival rates are similar to those in the general population of kidney transplant recipients.

Recent literature continues to address expanded criteria for transplantation for hepatocellular carcinoma, predictors of recurrence, the role of neoadjuvant therapy in patients with hepatocellular carcinoma, expanded donor criteria, transplantation and retransplantation for hepatitis C, and living donor transplantation. Further study is needed before liver transplant selection criteria can be expanded for hepatocellular carcinoma. Additionally, further study is needed to address salvage liver transplantation for HCC recurrence after primary liver resection.

Liver transplant for hilar cholangiocarcinoma is performed at some transplant centers and long-term survival has been reported in select patients with unresectable disease. For metastatic neuroendocrine tumors, cure of disease is not achieved and 5-year survival is generally not high. However, there have been reports of survival benefit in patients receiving liver transplantation for unresectable neuroendocrine tumor metastasis confined to the liver. Based on survival data and clinical vetting input, transplantation in patients with hilar cholangiocarcinoma who meet strict eligibility criteria may be considered medically necessary; transplantation for neuroendocrine tumors metastatic to the liver is considered investigational.

The literature on liver transplantation for pediatric hepatoblastoma is limited, but case series have demonstrated good outcomes and high rates of long-term survival. Additionally, nonmetastatic pediatric hepatoblastoma is included in UNOS criteria for patients eligible for liver transplantation. Therefore, liver transplantation for nonmetastatic pediatric hepatoblastoma may be considered medically necessary.

Case series have demonstrated favorable outcomes with liver retransplantation in certain populations, such as when criteria for an original liver transplantation are met for retransplantation. While some evidence suggests outcomes after retransplantation may be less favorable than for initial transplantation in some patients, long-term survival benefits have been demonstrated. There was support from clinical vetting for retransplantation following primary graft non-function, hepatic artery thrombosis, ischemic biliary injury after donation after cardiac death, chronic rejection or certain recurrent non-neoplastic diseases resulting in end-stage liver failure in a primary transplant. As a result, retransplantation after initial failed liver transplant may be considered medically necessary in these situations.

Billing/Coding/Physician Documentation Information

Liver Transplant

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable Codes: 47133, 47135, 47136, 47140, 47141, 47142, 47143, 47144, 47145, 47146, 47147, S2152

While charges for the retrieval of organs are considered eligible for coverage when patient criteria are met, any charges for the organ itself are considered ineligible for coverage.

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

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Independent Consultant Review - 2/99

Medical Policy Advisory Group - 12/99

Specialty Matched Consultant Advisory Panel - 10/2000

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Roland ME. Solid-organ transplantation in HIV-infected patients in the potent antiretroviral therapy era. Top HIV Med 2004; 12(3):73-6.

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Specialty Matched Consultant Advisory Panel 5/2013

Organ Procurement and Transplantation Network (OPTN). Organ Distribution: Allocation of Livers. 2013. Available online at: http://optn.transplant.hrsa.gov/PoliciesandBylaws2/policies/pdfs/policy_8.pdf. Last accessed March 2014.

National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Hepatobiliary Cancers; v1:2014 Available online at: http://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf. Last accessed March 2014.

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.03.06, 1/9/14

Specialty Matched Consultant Advisory Panel 5/2014

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.03.06, 1/15/15

Specialty Matched Consultant Advisory Panel 5/2015

Specialty Matched Consultant Advisory Panel 5/2016

Specialty Matched Consultant Advisory Panel 5/2017

Policy Implementation/Update Information

12/95	Local policy issued.
12/96	Reaffirmed.
11/98	Added statements from the National Association policy and Consultant reviews.
2/99	Independent Consultant Review
6/99	Reformatted, Description of Procedure or Service changed, Medical Term Definitions added.
12/99	Medical Policy Advisory Group
10/00	Specialty Matched Consultant Advisory Panel review. No change recommended in criteria. System coding changes. Medical Policy Advisory Group review. No change in criteria. Approve.

2/01	Revised. Added statements under the covered section. Added cadaver or living donor. Typo corrected.
2/03	Specialty Matched Consultant Advisory Panel review. No change to policy.
5/03	Description of Procedure or Service section expanded to provide more detail. General Criteria reformatted.
4/04	Benefits Application and Billing/Coding sections updated for consistency. Code S2152 added to Billing/Coding section.
9/9/04	Specialty Matched Consultant Advisory Panel review. No change to policy. Added new 2004 CPT codes 47140, 47141, 47142 to Billing/Coding section and removed code 47134 (code deleted, to report use 47140).
1/6/05	Codes 47143, 47144, 47145, 47146, 47147 added to the Billing/Coding section of policy.
10/2/06	Under "When Covered", A.1.b. "Viral hepatitis (all blood types)", now reads "Viral induced-hepatitis (all viral types)". Under "When Not Covered" 2. Contraindications, removed a. HIV- positive patient. Under "Policy Guidelines" C. Disease Specific Indications, 6.b. added "or HBeAg neg, HBV DNA pos,"; added 9. "HIV positivity: CD4 count >100cells/mm□; HIV-1 RNA undetectable; On stable anti-retroviral therapy >3 months; No other complications from AIDS (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidioses mycosis, resistant fungal infections, Kaposi's sarcoma, or other neoplasm); Meets all other criteria for transplantation. It is likely that each individual transplant center will have explicit patient selection criteria for HIV positive patients." Reference sources added. (pmo)
5/11/09	Under "When Not Covered", removed 3.a. Patients over age 70; added #4. "Certificate may exclude certain transplant services (e.g., artificial organs). Please refer to certificates for "Transplants Exclusions". Under "Policy Guidelines", B. Risk Factors, #2 now reads: "Nonhepatic neoplastic disease - patient must be off chemotherapy, determined to be disease free by usual monitoring studies, and have an expected 5-year survival rate of 80% or greater."; also added #7. "Advanced physiological age." Reference sources added. (pmo)
6/22/10	Policy Number(s) removed (amw)
5/24/11	Description section extensively revised. No change to the "When Liver Transplants Are Covered" section. Some information previously in the Covered/Not Covered sections was moved to the Benefits Application section. (adn)
5/29/12	Policy statements for medically necessary indications unchanged. Policy statements on hepatocellular carcinoma that has extended beyond the liver and ongoing alcohol and/or drug abuse moved from investigational to not medically necessary. Removed "Patients with an active infection" from the investigational policy statement. Potential contraindications added to Policy Guidelines. Specialty Matched Consultant Advisory Panel 5/16/12. (sk)
2/26/13	Reference added. Description section revised. Non-alcoholic steatohepatitis cirrhosis added to the medically necessary policy statement; a statement added that retransplantation may be considered medically necessary; a statement added that extrahepatic peri-hilar or hilar cholangiocarcinoma may be considered medically necessary. Information on other intrahepatic or extrahepatic malignancies including non-peri-hilar or non-hilar cholangiocarcinoma and recurrent hepatocellular carcinoma salvage treatment added to the Policy guidelines. Medical Director review. (sk)

5/28/13	Specialty Matched Consultant Advisory Panel 5/15/13. (sk)
4/1/14	References added. Policy Guidelines updated. Policy statement on polycystic liver disease moved to a separate policy statement. Pediatric non-metastatic hepatoblastoma added as may be medically necessary. Policy statement added that liver transplantation is considered investigational in all other situations not described. Senior Medical Director review. (sk)
6/10/14	Specialty Matched Consultant Advisory Panel 5/27/14. (sk)
3/31/15	Reference added. (sk)
7/1/15	Specialty Matched Consultant Advisory Panel 5/27/15. Removed related guidelines titled Therapeutic Apheresis and Radiofrequency Ablation of Primary or Metastatic Liver Tumors as these guidelines have been archived. (sk)
7/1/16	Specialty Matched Consultant Advisory Panel 5/25/16. (sk)
6/30/17	Specialty Matched Consultant Advisory Panel 5/31/17. (sk)