Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 1/1/24**
(See policy history boxes for previous effective dates)

Title: Transplant-Liver-Kidney (Combined)

Description/Background

A combined liver-kidney transplant (CLKT or LKTx), also known as a simultaneous liver-kidney transplant (SLK) may be an option for patients with end-stage disease in both the kidney and liver. Patients with hepatorenal syndrome receiving hemodialysis (HD) for more than two months, polycystic liver or kidney disease, or those with hyperoxaluria may be primary candidates for CLKT.

Prioritization of liver transplant candidates with renal dysfunction by the MELD (Model for End-Stage Liver Disease) system has resulted in a substantial increase in the number of simultaneous liver–kidney transplants. MELD is a numerical scale, ranging from 6 (less ill) to 40 (gravely ill), used for liver transplant candidates age 12 and older. It gives each person a 'score' (number) based on how urgently he or she needs a liver transplant within the next three months. The number is calculated by a formula using three routine lab test results: bilirubin, INR (prothrombin time) and serum creatinine. The only priority exception to MELD is a category known as Status 1. Status 1 patients have acute (sudden and severe onset) liver failure and a life expectancy of hours to a few days without a transplant. Less than one percent of liver transplant candidates are in this category. All other liver candidates age 12 and older are prioritized by the MELD system.

The introduction of MELD (model for end-stage liver disease) prioritization for liver transplant, which is greatly influenced by renal dysfunction, has coincided with an increase in simultaneous liver–kidney transplantation (SLK). SLK has increased from an average of 110 per year pre-MELD up to 368 in 2006 post-MELD.

In addition, there is a significant variability in the rate of SLK transplantation across the United States and Organ Procurement and Transplantation Network (OPTN) regions, which could be related to the acuity of patients on the waitlist in each region. This has raised concerns for two

reasons: (1) the incremental benefit attributable to the kidney transplant in SLK recipients is unknown and difficult to assess, and (2) SLK diverts deceased donor kidneys away from candidates for kidney transplant alone, which has created a vigorous debate about best use of organs and the ethical ramifications of allocating kidneys not only to liver-transplant candidates, but other extra renal transplant candidates as well.

Hepatorenal syndrome (a potentially reversible renal failure caused by liver disease) is end-stage disease of both the liver and kidneys and is usually caused by liver failure. Currently, hepatorenal syndrome combined with cirrhosis or another liver disease is often treated with liver transplant alone and not a combined liver/kidney transplant. Results of several studies show that varying degrees of renal failure in patients with chronic liver disease are associated with high mortality and morbidity after liver transplant alone.

Primary hyperoxaluria (sometimes referred to as oxalosis) is a genetic disorder that results in an increased production of oxalate by the liver. The large amount of oxalate leads to high concentrations in the urine, which, over time, can cause kidney stones and kidney failure. This disorder has two types, PH-I and PH-II (depending on the defective enzyme). Both types are rare. Patients who are unresponsive to vitamin B6 (pyridoxine) therapy will require combined liver and kidney transplantation. Long-term success with both transplants is good.

Another cause of end-stage kidney and liver disease is polycystic liver disease (PLD), a rare hepatic disorder and frequently associated with polycystic kidney disease (PKD). Hepatic cysts increase in frequency with aging and loss of renal function. This disease has autosomal dominant inheritance and is characterized by the presence of multiple scattered cysts of biliary origin in the liver parenchyma. Patients with adult polycystic kidney disease develop associated hepatic cysts in 34 to 78 percent of the time. Transplant of both kidney and liver is an excellent option with dramatic improvement in quality of life and acceptable morbidity.

The decision to transplant both the liver and kidney is more complicated in cases when kidney dysfunction may be temporary as it may be difficult to predict whether there will be sufficient return of native kidney function to recommend liver transplant alone. The model for end-stage liver disease (MELD) replaced the United Network for Organ Sharing status classification for the allocation of liver organs. Due to the heavily weighted serum creatinine value in the calculation of the MELD score, candidates with renal failure have received organs more rapidly. As a result, there has been considerable increase in nation-wide volume of combined liver-kidney transplants in the past three years.

There are currently no standard criteria for the evaluation of patients with acute kidney injury (AKI) or chronic kidney disease (CKD) requiring liver transplantation (LT). The decision to perform SLK (simultaneous liver-kidney) transplant is generally driven by concern over the likelihood of recovery of renal function and the associated increase in mortality in patients with non-recovery of renal function following liver transplantation alone (LTA). Because the persistence of preoperative renal dysfunction following LT has been associated with inferior patient survival, combined with the fact that kidney wait-list survival is comparatively worse for candidates with a previous LT, transplant programs often follow center-specific decision-making oriented toward ensuring adequate post-transplant renal function while considering the appropriateness of SLK. To this point, results of a recent survey completed by the Medical Directors of the Kidney Transplant Programs of US centers that perform SLK showed wide variability in criteria used for SLK and incongruity with the current published recommendations

or the proposed Organ Procurement and Transplantation Network (OPTN) listing criteria for SLK.

Consensus guidelines are not yet in place to clearly delineate indications for LKTx, but the Consensus Conference on Simultaneous Liver Kidney Transplantation Review Board has proposed the following indications: (1) end stage renal disease and symptomatic portal hypertension or hepatic vein wedge pressure gradient more than 10 mm Hg; (2) liver failure and CKD with GFR less than 30 mL/min; (3) AKI or HRS with creatinine more than 2.0 mg/dL and on dialysis more than 8 weeks; and (4) liver failure and CKD with renal biopsy demonstrating more than 30% glomerulosclerosis or 30% fibrosis.

Regulatory Status

N/A

Medical Policy Statement

Combined liver-kidney transplants have been clinically established as safe and effective for carefully selected individuals with end-stage disease in both organs.

Inclusionary and Exclusionary Guidelines

Note: Final patient eligibility for combined liver/kidney transplant is subject to the judgment and discretion of the requesting transplant center. Please refer to the Liver Transplant policy for full inclusionary criteria for liver transplant patients, and Kidney Transplant policy for full inclusionary criteria for kidney transplant patients.

Inclusions:
Indications for combined liver-kidney transplant include but are not limited to progressive chronic kidney/liver disease unresponsive to other medical and surgical therapy. In general, individuals are selected for combined kidney/liver transplant if one or more of the following apply:

- End-stage kidney and liver disease not amenable to any other form of therapy
- End stage liver disease and estimated glomerular filtration rate (eGFR) is 33 mL/minute or less, or preoperative evaluation of the kidney indicates the likelihood that the rate of progression of renal injury or dysfunction after single organ transplant is high
- Polycystic kidney and liver disease, primary hyperoxaluria and hepatorenal syndrome with terminal implications
- Fulminant or sub-acute hepatic/kidney failure

The consideration for risk-reducing procedure (e.g. CABG) performed at the same time as the organ transplant is a consideration based on the medical consultation review.

Exclusions

- Significant systemic or multisystemic disease (other than hepatorenal failure)
- 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 or enrollment in a sanctioned program)

- Malignancies metastasized to or extending beyond the margins of the liver and/or kidney.
- Individuals not meeting full inclusionary guidelines for liver transplant or renal transplant alone.

Potential contraindications for Transplant/Retransplant:
Note: Final patient eligibility for transplant is subject to the judgment and discretion of the requesting transplant center.

Potential contraindications represent situations where proceeding with transplant is not advisable in the context of limited organ availability. Contraindications may evolve over time as transplant experience grows in the medical community. Clinical documentation supplied to the health plan should demonstrate that attending staff at the transplant center have considered all contraindications as part of their overall evaluation of potential organ transplant recipients and have decided to proceed.

- Known current malignancy, or history of recent malignancy
- Untreated systemic infection making immunosuppression unsafe, including chronic infection
- Other irreversible end-stage disease not attributed to liver or kidney disease
- Systemic disease that could be exacerbated by immunosuppression
- Psychosocial conditions or chemical dependency affecting ability to adhere to therapy as defined by the transplant program

Liver Specific Guidelines for Alcohol Related Hepatitis

- Patients who are being considered for approval for a liver transplant who have liver disease related to alcohol use disorder must be evaluated for ongoing alcohol use.
- To determine candidacy for liver transplant in the setting of alcohol related hepatitis, guidelines such as the Dallas consensus criteria and the SALT criteria must be met. (see appendix for additional information).

All transplants must be prior authorized through the Human Organ Transplant Program

*Please note there are individual policies for each of these organs (liver transplant, kidney transplant) which contain more detailed information.

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

47135 50360 50365 47399

Other codes (investigational, not medically necessary, etc.):

N/A

Rationale

COMBINED LIVER-KIDNEY TRANSPLANTATION

Clinical Context and Therapy Purpose
The purpose of a combined liver-kidney transplantation for individuals who have indications for liver and kidney transplant is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following **PICO** was used to select literature to inform this review.

Populations
The relevant population of interest is individuals with indications for liver and kidney transplant.

Interventions
The therapy being considered is a combined liver-kidney transplantation

Comparators
The following tools and practices are currently being used to make decisions about managing combined liver-kidney transplantation: medical management or single organ transplant.

Outcomes
The general outcomes of interest are OS and treatment-related adverse events (e.g., immunosuppression, graft failure, surgical complications, infections). Short-term follow-up ranges from immediate post-surgery to 30 days post transplantation; lifelong follow-up (out to 10 years or more given current survival data) is necessary due to ongoing immunosuppression and risk of graft failure.

Review of Evidence
In simultaneous liver-kidney transplantation (SLK), the liver can protect the kidney from hyperacute rejection and may decrease acute cellular rejection rates. Whether the liver protects against chronic injury is unknown. To answer this Taner et al studied renal allograft surveillance biopsies in 68 consecutive SLK recipients (14 with donor-specific alloantibodies at transplantation [DSA+], 54 with low or no DSA, [DSA-]).[1] These were compared with biopsies of a matched cohort of kidney transplant alone (KTA) recipients (28 DSA+, 108 DSA-). Overall 5-year patient and graft survival was not different: 93.8% and 91.2% in SLK, and 91.9% and 77.1% in KTA. In DSA+ recipients, KTA had a significantly higher incidence of acute antibody-mediated rejection (46.4% vs. 7.1%) and chronic transplant glomerulopathy (53.6% vs. 0%). In DSA- recipients at 5 years, KTA had a significantly higher cumulative incidence of T cell-mediated rejection (clinical plus subclinical, 30.6% vs. 7.4%). By 5 years, DSA+ KTA had a 44% decline in mean GFR while DSA+SLK had stable GFR. In DSA- KTA, the incidence of a combined endpoint of renal allograft loss or over a 50% decline in GFR was significantly higher (20.4% vs. 7.4%). The authors concluded that simultaneously transplanted liver allograft was the most predictive factor for a significantly lower incidence of cellular (odds ratio 0.13, 95% confidence interval 0.06-0.27) and antibody-mediated injury (odds ratio 0.11, confidence interval 0.03-0.32), as well as graft functional decline (odds ratio 0.22, confidence interval 0.06-0.59). Thus, SLK is associated with reduced chronic cellular and antibody-mediated alloimmune injury in the kidney allograft.

Systematic Reviews

Bouari et al (2021) performed a systematic review and meta-analysis of 4 retrospective observational studies (N=22736) comparing survival and other outcomes among adult patients who received combined liver-kidney transplant to those with renal dysfunction who received liver transplant alone.[2] No significant difference in mortality was found between patients who received combined liver-kidney transplant and those who received liver transplant alone at 1 year (pooled risk ratio [RR], 1.03; 95% CI, 0.97 to 1.09; p=.31), 3 years (pooled RR, 1.06; 95% CI, 0.99 to 1.13; p=.11), or 5-years (pooled RR, 1.08; 95% CI, 0.98 to 1.19; p=.11) posttransplant. Pooled results from 2 studies showed that liver graft loss was not significantly different at 1 year, but was significantly increased at 3 years in patients who received liver transplant alone (RR, 1.15; 95% CI, 1.08 to 1.24; p<.0001). A single study reporting on liver graft survival at 5 years found no difference between groups.

Adults

In 2012, Fong et al evaluated data from the Organ Procurement Transplant Network (OPTN) and UNOS database to compare outcomes of combined liver-kidney transplantation (CLKT) with liver transplantation alone for adult cirrhotic patients with renal failure.[3] The analysis evaluated cirrhotic patients with serum creatinine level 2.5 mg/dL or higher or who received dialysis at least twice during the week before liver transplantation. Between 2002 and 2008, 2774 patients had both liver and renal failure and received a liver transplant alone and 1501 patients who underwent CLKT. Patients who received the CLKT were more likely to be over 60 years of age, have minimal liver disease, and have been on dialysis. Patients in the combined transplant group were also not as sick, with fewer patients who had a MELD score over 35 at listing, fewer who were hospitalized prior to transplant, and fewer who were on life support. Liver and patient survival were higher in patients who received CLKT compared with liver transplant alone. At 5 years post-transplant, 67.4% of patients had survived in the CLKT arm compared with 62.9% in the liver alone arm (p<0.001 over 5 years). The liver allograft survival after 5 years was 65.3% in the CLKT arm and 58.9% in the liver transplantation alone (p<0.001). After adjusting for confounding factors, liver transplant alone remained a significant risk factor for liver allograft loss (HR=1.24, p=0.002) and mortality compared with CLKT transplantation (HR=1.16, p=0.043).

In a 2017 retrospective study, Lunsford et al evaluated factors for renal failure in patients who underwent CLKT.[4] Out of 145 patients who underwent CLKT, 30 (20.7%) had renal failure. Survival at 1 and 3 years in the CLKT group with renal failure (18.2% and 13.5%) was significantly worse than in CLKT patients without renal failure (92.6% and 83.7%, p<0.001). Multivariate predictors of renal failure were pretransplant dialysis duration (Odds ratio [OR] 2.43 per log SD, p=0.008), kidney cold ischemia of more than 883 minutes (OR 3.43, p=0.011), kidney donor risk index (OR 1.96 per log SD, p=0.012), and recipient hyperlipidemia (OR 3.50, p=0.028).

In a 2010 (Ruiz et al) series of 74 CLKT procedures performed at a single institution over a 23-year period, survival was 62% at 5 years.[5] However, in patients who were undergoing a second CLKT or liver retransplantation, survival was 30% at 3 months. This led to a recommendation to not perform CLKT in patients requiring liver retransplantation. There was no significant difference in survival between patients who were on hemodialysis pretransplantation and those who were not. However, survival in patients who required hemodialysis after transplantation was significantly worse (≈30% at 5 years) than for patients

who did not (≈70%, p=0.001 over follow-up), and kidney graft survival was only 56% at 5 years.

Children

In 2014, Calinescu et al evaluated outcomes of CLKT in children using the Scientific Registry of Transplant Recipients from OPTN.[6] There were 152 primary CLKTs performed in the period between 1987 and 2011. Liver graft survival was 72.6% at 10 years and kidney graft survival was 66.9%. Patient survival at 10 years after CLKT was 78.9%. In comparison, patient survival following isolated liver transplantation during the same period was 77.4% (n=10,084), and for isolated kidney transplant, 90% at 10 years (n=14,800). Thus, CLKT resulted in survival outcomes that were no worse than liver transplant alone, but were inferior to kidney transplant alone. Indications for CLKT were noted as primary hyperoxaluria and other liver-based metabolic abnormalities affecting the kidney, along with structural diseases affecting both the liver and kidney such as congenital hepatic fibrosis and polycystic kidney disease. A table of the indications for CLKT in children treated between 1987 and 2011 is included in this publication.

Some reports have suggested that liver transplantation may have a protective effect on kidney allografts. To test this hypothesis, de al Cerda et al (2010) evaluated kidney survival in children who had kidney only or CLKT.[7] Examination of the OPTN/UNOS database between 1995 and 2005 identified 111 combined liver-kidney transplantations and 3798 kidney only transplants in children. The patients in the CLKT group were younger on average (9 years vs. 12 years, p=0.007) and more had inherited disease as the primary cause (42% vs. 28%). More patients in the combined liver-kidney transplantation group lost their kidney graft within 6 months (20.1% vs. 5.9%, p=0.001), however, late kidney graft survival was significantly better at 5 years post-transplant compared with the kidney only group (p<0.01). The authors described 2 situations when combined liver-kidney transplant would be indicated in children: end-stage liver disease when the kidneys go into prolonged irreversible failure, and severe renal failure from an underlying disease that can be improved with liver transplant.

SUMMARY OF EVIDENCE

The evidence on CLKT includes a systematic review of retrospective observational studies in adult patients and several registry studies that compare combined organ transplantation with liver or with kidney transplantation alone. In adults undergoing liver transplant with kidney failure, CLKT results in a modest improvement in patient survival compared with liver transplantation alone. Liver allograft survival was also higher in the patients who received CLKT compared with patients who received a liver transplant alone. There are relatively few children who have received CLKT. Patient survival has been reported to be worse than following kidney transplantation alone, but no worse than for liver transplant alone. For kidney grafts that survive the first 6 months, organ survival may be better than for a kidney graft alone. Together, these results would suggest that CLKT is no worse, and possibly better for, graft and patient survival in adults and children who meet the requirements for liver transplantation and have concomitant renal failure. Indications for CLKT in children are rare and often congenital, and include liver-based metabolic abnormalities affecting the kidney, along with structural diseases affecting both the liver and kidney.

SUPPLEMENTAL INFORMATION

PRACTICE GUIDELINES AND POSITION STATEMENT

Organ Procurement and Transplantation Network

The Organ Procurement and Transplantation Network's new prioritization guidelines for simultaneous liver-kidney allocation became effective August 10, 2017.[15] The listed medical eligibility requirements related to kidney function are required for an adult liver-kidney candidate to receive a liver and kidney transplant from the same deceased donor.[16]

Current OPTN/UNOS policy prioritizes candidates seeking a simultaneous liver kidney (SLK) transplant *before* pediatric and adult transplant candidates who are listed only for a kidney ("kidney alone candidates") when the liver candidate and the deceased donor are in the same Donation Service Area (DSA). Unlike kidney alone allocation, in SLK allocation, the kidney is not allocated based on medical criteria assessing the kidney function of the candidate. Instead, geographic proximity between the liver-kidney candidate and the donor is the single factor for allocating the kidney with the liver. Organ procurement organizations (OPOs) are not required to allocate the kidney with the liver to a *regional* SLK candidate, although they have the discretion to do so.

The Kidney Transplantation Committee ("the Committee"), has identified several problems with this current policy:

- The current policy for SLK allocation is counter to requirements in the OPTN Final Rule ("Final Rule") specifying that organ allocation policies be based on sound medical judgment and standardized criteria.
- The lack of medical criteria results in the allocation of high quality kidneys to liver candidates who may regain renal function after liver transplant and decreased access for kidney alone candidates who would otherwise be highly prioritized in deceased donor kidney allocation.
- The lack of consistency for regional SLK allocation has been a tremendous concern for the liver transplant community, as deceased donor liver allocation prioritizes candidates with a certain medical urgency status or Model End Stage Liver Disease Score (MELD) score or Pediatric End Stage Liver Disease (PELD) score for regional allocation but regional liver-kidney allocation is not required for these candidates.

In order to provide more clarity and consistency in the rules for liver-kidney allocation, the Committee is proposing a second round of public comment on this proposal which consists of the following:

- Establish medical eligibility criteria for adult candidates seeking an SLK transplant.
- Provide greater clarity for the rules around liver-kidney allocation and fix the inconsistency that exists between deceased donor liver allocation policy and liver-kidney allocation policy.
- Establish a "safety net" (new match classification priority on the kidney alone waiting list) for liver recipients with continued dialysis dependency or kidney dysfunction in the first year after liver transplant as an added element to address concerns about limitations associated with the SLK medical eligibility criteria.

ONGOING AND UNPUBLISHED CLINICAL TRIALS

Some currently unpublished trial that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT03100682	Prevention of HPV infection in pediatric kidney and liver transplant recipients and in pediatric patients with advanced chronic kidney disease.	140	Dec 2022

NCT: national clinical trial

Government Regulations
National/Local:

There is no national or local coverage determination addressing a combined liver/kidney transplant. However, Medicare does provide coverage for individual liver and kidney transplant.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [BCBSM, formerly HCFA] are updated and/or revised periodically. Therefore, the most current BCBSM CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Heart Transplant
- Heart/Lung Transplant
- Heart-Kidney Combined Transplant
- Liver Transplant
- Lung and Lobar Lung Transplant
- Lung-Double Lung and Liver Transplant
- Pancreas Transplant
- Small Bowel /Liver and Small Bowel/Multivisceral Transplant
- Small Bowel Transplant-Isolated

References

1. Taner T, Heimbach JK, Rosen CB, et al. Decreased chronic cellular and antibody-mediated injury in the kidney following simultaneous liver-kidney transplantation. Kidney Int. 2016;89(4):909-917.
2. Bouari S, Rijkse E, Metselaar HJ, et al. A comparison between combined liver kidney transplants to liver transplants alone: A systematic review and meta-analysis. Transplant Rev (Orlando). Jun 01 2021; 35(4): 100633. PMID 34098490
3. Fong TL, Khemichian S, Shah T, Hutchinson IV, Cho YW. Combined liver-kidney transplantation is preferable to liver transplant alone for cirrhotic patients with renal failure. Transplantation. 2012 Aug 27;94(4):411-6.

4. Lunsford KE, Bodzin AS, Markovic D, et al. Avoiding Futility in Simultaneous Liver-kidney Transplantation: Analysis of 331 Consecutive Patients Listed for Dual Organ Replacement. *Ann Surg.* May 2017;265(5):1016-1024. PMID 27232249
5. Ruiz R, Jennings LW, Kim P, et al. Indications for combined liver and kidney transplantation: propositions after a 23-yr experience. *Clin Transplant.* Nov-Dec 2010;24(6):807-811. PMID 20002463
6. Calinescu AM, Wildhaber BE, Poncet A, et al. Outcomes of combined liver-kidney transplantation in children: analysis of the scientific registry of transplant recipients. *Am J Transplant.* Dec 2014;14(12):2861-2868. PMID 25274400
7. de la Cerda F, Jimenez WA, Gjertson DW, et al. Renal graft outcome after combined liver and kidney transplantation in children: UCLA and UNOS experience. *Pediatr Transplant.* Jun 2010;14(4):459-464. PMID 20070563
8. Haad CR, Rodriguez-Benot A, Martinez-Vaquera S, Navarro-Cabello MD, Aguera-Morales ML, Ruiz de Mier MV, Montero-Alvarez JL, Mata-Garcia Mde L, Briceño-Delgado J, Aljama-Garcia P. Combined liver-kidney transplantation: survey of a single center in Spain. Transplant Proc. 2013 Dec;45(10):3640-3.
9. Martin EF, Huang J, Xiang, Q, Klein JP, Bajaj J, and Kia Saeian. Recipient Survival and Graft Survival are Not Diminished by Simultaneous Liver-Kidney Transplantation: An Analysis of the United Network for Organ Sharing Database. Liver Transplantation. Volume 18, Issue 8, pp 914-first published online 24 JUL 2012. Available at http://onlinelibrary.wiley.com/doi/10.1002/lt.23440/pdf (Accessed 9/1/17).
10. Martin P, DiMartini A, Feng S, Brown Robert Jr, Fallon M. AASLD 2013 Practice Guideline: Evaluation for Liver Transplantation in Adults: Recommendations and Rationales. Available at http://www.aasld.org/sites/default/files/guideline_documents/evaluationadultltenhanced.pdf (Accessed 9/1/17).
11. Nadim MK, Sung RS, Davis CL, Andreoni KA, Biuggins SW, Danovitch GM, Feng S, Firedewald JJ, Hong JC, Kellum JA, Kim WR, Lake JR, Melton LBs, Pomfret EA, PomfretS, Saab S, Genyk YS. Simultaneous Liver–Kidney Transplantation Summit: Current State and Future Directions. American Journal of Transplantation. 2012;12(11):2901-2908.
12. Papafragkakis H, Martin P, Akalin E. Combined liver and kidney transplantation. Curr Opin Organ Transplant. 2010 Jun;15(3):263-8.
13. Pham Phuong-Thus T. and Pham Phuong-Chi T. Clinical Decision-Making Dilemna: Liver alone or Simultaneous Liver- Kidney Transplantation? J Transplant Technol Res 2012, 2:3.
14. Xing T, Zhong L, Chen D, Peng Z. Experience of combined liver-kidney transplantation for acute-on-chronic liver failure patients with renal dysfunction. Transplant Pro. 2013 Jul-Aug;45(6):2307-13.
15. Organ Procurement and Transplantation Network. Simultaneous Liver and Kidney allocation. 2016; https://optn.transplant.hrsa.gov/governance/public-comment/simultaneous-liver-kidney-allocation-2016/. Accessed September 2023.
16. Organ Procurement and Transplantation Network. Simultaneous liver kidney allocation: Briefing paper. 2016; https://optn.transplant.hrsa.gov/media/1871/kidney_briefingpaper_slk_201606.pdf. Accessed September 2023.
17. Asrani SK, Trotter J, Lake J, et al. Meeting report: the DALLAS consensus conference on liver transplantation for alcohol related hepatitis. Liver Transpl. Jan 2020; 26(1):127-140
18. Lee BP, Vittinghoff E, Hsu C, et al. Predicting low-risk for sustained alcohol use after early liver transplant for acute alcoholic hepatitis: the SALT score. Hepatology. Apr 2019; 69(4):1477-1487

19. Chadban SJ, Ahn C, Axelrod DA, et al. KDIGO clinical practice guideline on the evaluation and management of candidates for kidney transplantation. Transplantation. 2020; 104:S1-S103.

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through September 2023, the date the research was completed.

Appendix:

DALLAS Consensus Statement on Liver Transplantation for Alcohol Related Hepatitis[17]

SUMMARY OF RECOMMENDATIONS
General recommendations: Alcohol related hepatitis

1. There should be efforts to standardize nomenclature and definition of alcohol related hepatitis (AH) with an emphasis on use of less stigmatizing terminology.
2. Patients with severe AH may be assessed for corticosteroid therapy.
3. Select patients with severe AH that are unresponsive or ineligible for medical management may be considered for liver transplantation.
4. Predicting response to therapy or pre-LT mortality is best achieved by assessing response over time (change in Model for end stage liver disease (MELD) score, Lille score or a combination of MELD score plus Lille). Mortality is lower for those that have a Lille score <0.45, respond to therapy, have a declining bilirubin, or are abstinent and these patients may not require LT.
5. An inflexible period of abstinence prior to transplantation is not desirable. Acceptance for LT listing should be based upon the severity of liver dysfunction and a comprehensive psychosocial evaluation.

Recommendations for LT for alcohol related hepatitis

A. The goals of LT for AH include:
1. Avoiding LT in patients who will recover without it
2. Avoiding futility and achieving short- and long-term survival comparable to other indications for LT
3. Avoiding creation of further disparity in LT either by indication (versus other indications), geography, sex, race, insurance status or other sociodemographic factors.
4. Identification of LT candidates likely to have long-term abstinence
5. Incorporation treatment of alcohol use disorder (AUD) into pre and post-LT care
6. Consensus of paramedical and medical staff
B. Criteria related to AH
1. First presentation with decompensated alcohol-related liver disease
2. Absence of severe uncontrolled medical or psychiatric comorbidities.
3. Non-response to or ineligible for medical therapy.
C. Criteria related to AUD
1. Establish acceptable risk of relapse by assessment with a multidisciplinary psychosocial team including a social worker and an addiction medicine specialist/mental health professional with addiction and transplantation expertise.
2. Assessment of coherent patient by addiction specialist (i.e. not

intubated or floridly encephalopathic).
3. Lack of repeated unsuccessful attempts at addiction rehabilitation.
4. Lack of current other substance use/dependency.
5. Acceptance of ALD diagnosis with insight.
6. Commitment of patient to lifelong sobriety and support of sober caregivers to assist patient with abstinence goals.
7. Presence of close, supportive family members or caregivers

D. Post LT requirements
1. Pre-LT confirmation of plan for AUD treatment after LT
2. Robust post-transplant monitoring for alcohol slips or relapse during post-LT clinic appointments to include direct interviewing of patient and caregivers about alcohol use.
3. Routine monitoring of alcohol use (e.g. with Phosphatidylethanol (PEth), Urinary ethyl glucuronide) for at least 2 years, with frequency and duration individualized beyond this time period.

E. Center requirements
1. Transparency in the candidate selection process and structured collection of objective data to assess outcomes
2. Ongoing support of abstinence that is integrated into post LT care such as concurrent follow-up by addiction specialist/mental health professional with addiction and transplantation expertise.
3. Oversight of program adherence to harmonize listing practices and outcomes.

LT: liver transplant; AH: alcohol related hepatitis; AUD: alcohol use disorder; Peth: phosphatidylethanol; ETG: urinary ethyl glucuronide

The SALT Score

SALT Score to Predict Sustained Alcohol Use Post-LT[18]

Variable	Points
>10 Drinks/day at Presentation	+4
≥2 Prior Failed Rehabilitation Attempts	+4
Any History of Prior Alcohol-Related Legal Issues	+2
History of Non-THC Illicit Substance abuse	+1

The SALT Score was generated from a full LASSO logistic point-score model to predict sustained alcohol use post-LT. The score assigns points to variables which were associated with sustained alcohol use post-LT, and ranges 0–11. Using a cutoff of 5, the SALT score had a c-statistic estimate of 0.76 to predict sustained alcohol use post-LT.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
11/1/07	11/2/07	10/30/07	Joint policy established
11/1/08	8/19/08	10/28/08	Routine maintenance
3/1/10	12/8/09	12/8/09	Routine maintenance
1/1/13	10/16/12	10/16/12	Routine maintenance
9/1/14	6/20/14	6/23/14	Routine update of established service. No change in policy status.
9/1/15	6/19/15	7/16/15	Routine update of established service. No change in policy status.
9/1/16	6/21/16	6/21/16	Routine policy update. No changes in policy status. Recommend retirement.
3/1/17	12/13/16	12/13/16	Deleted code 47136, added code 47399. Deleted reference to Blue Cross Complete.
3/1/18	12/12/17	12/12/17	Updated rationale, added reference # 2-6. No change in policy status.
3/1/19	12/11/18		Routine policy maintenance, added reference # 14 and 15. No change in policy status.
3/1/20	12/17/19		Policy inclusions/exclusions updated, no change in policy status.
3/1/21	12/15/20		Routine policy maintenance, no change in policy status.
1/1/22	10/19/21		Rationale updated, reference #2 added, no change in policy status.
1/1/23	10/18/22		Routine policy maintenance, no change in policy status.
1/1/24	10/26/23		Added statement to inclusion section. Appendix added to policy on DALLAS consensus statement and on SALT score. Title changed to start with “Transplant”. Routine policy maintenance, no change in policy status. Vendor managed: N/A (ds)

Next Review Date: 4th Qtr. 2024

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: TRANSPLANT-LIVER/KIDNEY (COMBINED)

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered; criteria apply. Transportation, meals and lodging expenses related to the transplant are not covered unless specifically noted in the member's certificate/rider.
BCNA (Medicare Advantage)	See government section.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

Note: All services related to the transplant, except evaluation services, will not be authorized until the transplant is approved.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.