Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 5/1/25**
(See policy history boxes for previous effective dates)

Title: Transplant-Heart-Lung (Combined)

Description/Background

Solid organ transplantation offers a treatment option for patients with different types of end-stage organ failure that can be lifesaving or provide significant improvements to a patient's quality of life.[2] Many advances have been made in the last several decades to reduce perioperative complications. Available data supports improvement in long-term survival as well as improved quality of life particularly for liver, kidney, pancreas, heart, and lung transplants. Allograft rejection remains a key early and late complication risk for any organ transplantation. Transplant recipients require life-long immunosuppression to prevent rejection. Patients are prioritized for transplant by mortality risk and severity of illness criteria developed by Organ Procurement and Transplantation Network and United Network of Organ Sharing.

Most heart-lung transplant recipients have Eisenmenger syndrome (37%), followed by idiopathic pulmonary artery hypertension (28%) and cystic fibrosis (14%). Eisenmenger syndrome is a form of congenital heart disease in which systemic-to-pulmonary shunting leads to pulmonary vascular resistance. It is possible that pulmonary hypertension could lead to a reversal of the intracardiac shunting and inadequate peripheral oxygenation or cyanosis.[3]

Heart-lung Transplant
Combined heart-lung transplantation is intended to prolong survival and improve function in patients with end-stage cardiac and pulmonary diseases. Due to corrective surgical techniques and improved medical management of pulmonary hypertension, the total number of patients with Eisenmenger syndrome has seen a decline in recent years. Additionally, heart-lung transplants have not increased appreciably, but for other indications, it has become more common to transplant a single or double lung and maximize medical therapy for heart failure, rather than perform a combined transplant. For those indications, patient survival rates following heart-lung transplantations are similar to lung transplant rates. Bronchiolitis obliterans syndrome is a major complication. One-, 5-, and 10-year patient survival rates for heart-lung

transplants performed between 1982 and 2014 were estimated at 63%, 45%, and 32%, respectively.[4]

Regulatory Status:

Solid organ transplants are a surgical procedure and, as such, are not subject to regulation by the U.S. Food and Drug Administration. The U.S. Food and Drug Administration regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation Title 21, parts 1270 and 1271. Solid organs used for transplantation are subject to these regulations.

Medical Policy Statement

Combined heart-lung transplantation has been clinically established. It may be considered a useful therapeutic procedure for carefully selected individuals when criteria are met.

Inclusionary and Exclusionary Guidelines

Note: Final patient eligibility for combined heart-lung transplant is subject to the judgment and discretion of the requesting transplant center. Please refer to the heart Transplant policy for full inclusionary criteria for heart transplant patients, and Lung/double lung transplant policy for full inclusionary criteria for lung transplant patients.

Inclusions:
Heart-lung transplantation may be indicated in individuals who qualify for combined heart-Lung transplantation and have advanced irreversible heart and lung disease.

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

- Irreversible primary pulmonary hypertension with heart failure;
- Nonspecific severe pulmonary fibrosis, with severe heart failure;
- Eisenmenger complex with irreversible pulmonary hypertension and heart failure;
- Cystic fibrosis with severe heart failure;
- Chronic obstructive pulmonary disease with heart failure;
- Emphysema with severe heart failure;
- Pulmonary fibrosis with uncontrollable pulmonary hypertension or heart failure.

Heart-lung retransplantation after a failed primary heart-lung transplant may be considered established in individuals who meet selection criteria for heart-lung retransplantation.

Exclusions

- Heart-lung transplantation is considered investigational in all other situations.

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, including metastatic cancer;
- Recent malignancy with moderate or high risk of recurrence;
- History of cancer with a moderate risk of recurrence;
- Untreated systemic infection making immunosuppression unsafe, including chronic infection;
- Other irreversible end-stage disease not attributed to heart or lung disease;
- Systemic disease that could be exacerbated by immunosuppression;
- Psychosocial conditions or chemical dependency affecting ability to adhere to therapy.

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

*Please note there are individual policies for each of these organs (heart transplant, lung 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:

33930 33933 33935

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

N/A

Rationale

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be

relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Due to the nature of the disease condition, there are no randomized controlled trials comparing heart-lung transplant with alternatives. Systematic reviews are based on case series and registry data. The extant randomized controlled trials compare surgical technique, infection prophylaxis, and immunosuppressive therapy and are not germane to this evidence review.

Prioritization of Candidates

Individuals who are eligible for heart-lung transplantation can be listed under both the heart and lung allocation systems in the United States. In 2005, UNOS changed the method by which lungs were allocated, from one based on length of time on the waiting list, to a system that incorporates the severity of the patient's underlying disease, as well as likelihood of survival.[7] However, it has been noted that the individual systems underestimate the severity of illness in patients with both end-stage heart and lung failure, and modification of the lung allocation score can be appealed for patients who meet the following criteria:[8]

- Deterioration on optimal therapy
- Right arterial pressure greater than 15 mm Hg
- Cardiac index less than 1.8 L/min/m^2

Specific criteria for prioritizing donor thoracic organs for transplant are provided by the Organ Procurement and Transplantation Network (OPTN) and implemented through a contract with UNOS.[6]

Yusen et al (2016) conducted an analysis of the heart-lung transplantations performed among adults during 1982-2015 using the ISHLT registry database.[4] Among the 3397 heart-lung transplants during that period for whom diagnosis was reported, 35% had congenital heart disease, 27% had pulmonary arterial hypertension and 14% had cystic fibrosis as the primary indication. There was a shift in indications for heart-lung transplantation over time. During 2004-2015, congenital heart disease (35%), pulmonary arterial hypertension (27%) and cardiomyopathy (11%) were the three most common indications for heart-lung transplantation. Of the 883 heart-lung transplant recipients during 2004-2015, 36% were 18-34 years of age, 40% were 35-49 and 24% were 50 years or older.

Pediatric Considerations

In an analysis of data from the OPTN, Spahr and West (2014) provided indications for pediatric heart-lung transplantation.[9] The number of pediatric heart-lung transplants has decreased in recent years (56 cases from 1993 to 1997; 32 cases from 2008 to 2013). The 3 most common indications for pediatric heart-lung transplant were primary pulmonary hypertension (n=55), CHD (n=37), and Eisenmenger syndrome (n=30). However, while 30 children received a heart-lung transplant for Eisenmenger syndrome through 2002, no transplants for this syndrome have been performed since then. Pediatric heart-lung transplants have also been performed

for other indications, including alpha1-antitrypsin deficiency, pulmonary vascular disease, cystic fibrosis, and dilated cardiomyopathy.

Using ISHLT Registry data, Benden et al (2012) reported on pediatric heart-lung transplant data collected through June 2011.[10] Overall survival rates after heart-lung transplants are comparable in children (median half-life, 4.7 years) and adults (median half-life, 5.3 years). For pediatric heart-lung transplants performed between 1990 and 2010, the 5-year survival rate was 49%. The 2 leading causes of death in the first year after transplantation were noncytomegalovirus infection and graft failure. Beyond 3 years posttransplant, the major cause of death was bronchiolitis obliterans syndrome. An updated report by Benden et al (2014) on pediatric lung and heart-lung transplant from the same registry did not include updated data on pediatric heart-lung transplants due to the small number of patients available.[11]

INITIAL HEART-LUNG TRANSPLANTATION

Clinical Context and Therapy Purpose

The purpose of combined heart-lung transplant in individuals who have end-stage cardiac and pulmonary disease is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following **PICOs** were used to select literature to inform this review.

Populations

The relevant population of interest is individuals with end-stage cardiac and pulmonary disease.

Interventions

The therapy being considered is combined heart-lung transplant.

Comparators

The following practices are currently being used to make decisions about end-stage cardiac and pulmonary disease: medical management, double-lung transplant, and single-lung transplant.

Outcomes

The general outcomes of interest are overall survival, graft failure, improved function, and adverse events (e.g., infections).

Follow-up after surgery focuses on monitoring for graft failure. Long-term follow-up can continue out to 3 to 5 years and beyond.

Review of Evidence

Yan et al (2023) conducted a systematic review comparing outcomes between bilateral lung transplantation and heart-lungtransplantation.[11] The authors identified 10 cohort studies (N=2252) for inclusion. There were no significant differences between groups in survival at 1 year (risk ratio [RR], 1.05; 95% CI, 1.00-1.11; p=.06), 3 years (RR, 1.06; 95% CI, 0.98-1.15; p=.13), 5years (RR, 1.02; 95% CI, 0.92-1.13; p=0.71), or 10 years (RR, 1.03; 95% CI, 0.90-1.19, p=.68). Other outcomes including chronic lung allograft dysfunction-free survival, hospital stay, in-hospital mortality, and surgical complications were also similar between groups.

Registry Studies and Case Series

Sertic et al (2020) compared outcomes of bilateral lung transplantation with cardiac defect repair to combined heart-lung transplantation in adult patients with Eisenmenger's syndrome using the United Network for Organ Sharing (UNOS) database of heart-lung transplantations performed from 1987 to 2018.[12] Among 442 patients who underwent thoracic transplantation, 316 patients underwent heart-lung transplantation and 126 patients underwent double-lung transplantation with concomitant cardiac defect repair. Overall survival was similar between patients who underwent double-lung transplantation and those who underwent heart-lung transplantation at 1 year (63.1% vs. 68.0%, respectively), 5 years (38.5% vs. 47.3%), and 10 years (30.2% vs. 30.5%) posttransplant (p=0.6). Overall survival did not differ among patients who received transplantation between 1987 to 1999 and those who received transplantation between 2000 to 2018 (p=0.7).

Yusen et al (2016) reported the survival of adult heart-lung transplant recipients using the ISHLT database.[3] Among the 3775 primary heart-lung transplants performed during 1982 to 2014, the 3 months, 1 year, 3 years, 5 years and 10 years survival rates were 71%, 63%, 52%, 45%, and 32% respectively. The overall median survival during this period (1982-2014) was 3.4 years. Those who survived to 1 year had a conditional median survival of 10.3 years. Survival improved over time, with median survival of 2.1 years for the patients who received transplant during 1982 to 1993 (n=1596), 3.9 years for patients during 1994 to 2003 (n=1392), and 5.8 years for patients during 2004 to 2014 (n=843) (p<0.05 for all pair wise comparisons). Heart-lung transplant recipients in the 2004 to 2014 group had a median conditional survival beyond 10 years. Compared with lung-only transplantation (median conditional survival, 8.0 years), heart-lung transplant recipients had a better long-term survival (median conditional survival, 10.3 years).

Hill et al (2015) compared survival following heart-lung transplantation with double-lung transplantation for idiopathic pulmonary arterial hypertension (IPAH) among adult transplant recipients in the Scientific Registry of Transplant Recipients (SRTR) database during 1987-2012.[13] Among the 928 IPAH patients, 667 underwent double-lung transplantation and 261 underwent heart-lung transplantation. Overall, the adjusted survival was similar between double-lung transplantation and heart-lung transplant recipients. However, for recipients who were hospitalized in the ICU, double-lung transplantation was associated with worse outcome compared to heart-lung transplantation recipients (hazard ratio [HR], 1.83; 95% confidence interval [CI], 1.02 to 3.28).

Jayarajan et al (2014) compared the mortality at 1 month and 5 year post transplant between heart-lung transplant recipients requiring pretransplant ventilation (n=22) or extracorporeal membrane oxygenation (ECMO) (n=15) and evenly matched controls.[14] Median survival was 10 days, 181 days, and 1547 days among patients with pretransplant ECMO, patients with mechanical ventilator and control group, respectively. Patients with pretransplant ECMO had a worse survival than the control group at 30 days (20.0% vs. 83.5%) and 5 years (20.0% vs. 47.4%; p<0.001). Similarly patients requiring ventilation prior transplantation had worse survival at 1 month (77.3% vs. 83.5%) and 5 years (26.5% vs. 47.4%; p<0.001) compared with the control group. The use of ECMO (HR=3.82; 95% CI, 1.60 to 9.12; p=0.003) or mechanical ventilation (HR=2.01; 95% CI, 1.07 to 3.78; p=0.030) as a bridge to transplantation was independently associated with mortality on multivariate analysis. The findings of the study raises question whether combined heart-lung transplant should be carried out in patients

requiring ECMO and suggests a need for further research to improve survival in this high risk group of patients.

Pediatric Considerations
Riggs et al (2020) assessed outcomes for pediatric heart-lung transplantation among children with congenital heart disease (CHD) with Eisenmenger syndrome, CHD without Eisenmenger syndrome, primary pulmonary hypertension, and "other" categories using the UNOS database of heart-lung transplantations performed from 1987 to 2018.[15] Among 209 heart-lung transplantations performed during the specified time frame, 37 (17.7%) had CHD with Eisenmenger syndrome, 40 (19.1%) had CHD without Eisenmenger syndrome, 70 (33.5%) had primary pulmonary hypertension, 6 (2.9%) were retransplants, and 56 (26.8%) had another diagnosis. One-year, 5-year, and 10-year survival rates post-transplant, respectively, were 75%, 44%, and 32% for pediatric patients with CHD with Eisenmenger syndrome, 56%, 21%, and 16% for patients with CHD without Eisenmenger syndrome, 77%, 41%, and 33% for patients with primary pulmonary hypertension, 40%, 0%, and 0% for retransplanted patients, and 70%, 44%, and 20% for patients with other diagnoses. Compared to the reference group of pediatric patients with primary pulmonary hypertension, patients with CHD without Eisenmenger syndrome (p=0.03) and patients who were retransplanted (p=0.008) had significantly lower survival rates. Other survival comparisons were not significant. Survival rates were not different when comparing patients who received transplants between 1987 to 1999 and 2000 to 2018. Infants (HR, 2.2; 95% CI, 1.04 to 4.55; p=0.04), 1 to 11 year old patients (HR, 1.78; 95% CI, 1.12 to 2.8; p=0.015), and patients on ECMO (HR, 4.1; 95% CI, 1.3 to 12.8; p=0.016) had the highest risk of mortality post-transplant.

Goldfarb et al (2016) reported the survival of pediatric lung and heart-lung transplant recipients using the ISHLT database.[16] Among the 698 pediatric heart-lung transplant recipients, median survival was 3.0 years and conditional median survival was 7.8 years. There was no statistically significant difference in survival by indication, recipient age group or era (time period) of transplant for pediatric heart-lung transplant recipients.

Section Summary: Initial Heart-lung Transplant
Data from transplantation registries have found increasing patient survival rates after initial heart-lung transplant among adult and pediatric patients over time. Net benefit of heart transplantation compared to lung-only transplantation is also evident, especially among patients with idiopathic pulmonary arterial hypertension.

HEART-LUNG RETRANSPLANTATION

Clinical Context and Therapy Purpose
The purpose of combined heart-lung retransplant in individuals who have had a combined heart-lung transplant complicated by graft failure or severe dysfunction of the heart-lung is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following **PICOs** were used to select literature to inform this review.

Populations
The relevant population of interest is individuals with a combined heart-lung transplant complicated by graft failure or severe dysfunction of the heart-lung.

Interventions
The therapy being considered is combined heart-lung retransplant.

Comparators
The following practices are currently being used to make decisions about a combined heart-lung transplant complicated by graft failure or severe dysfunction of the heart-lung: medical management, double-lung transplant, and single-lung transplant.

Outcomes
The general outcomes of interest are overall survival, graft failure, improved function, and adverse events (e.g., infections).

Follow-up after surgery focuses on monitoring for graft failure. Long-term follow-up can continue out to 3 to 5 years and beyond.

Review of Evidence

Registry Studies
Repeat heart-lung transplant procedures have been performed. In 2014, Yusen et al reported outcomes for adult heart-lung transplants, with a focus on retransplantation, using data from the ISHLT Registry.[17] From 1982 to 2012, 90 adults had a first heart-lung retransplant after a previous heart-lung transplant. These 90 patients had a median survival of 0.3 year, with an unadjusted survival rate of 52%, 43%, 36%, and 27% at 3 months, 1 year, 3 years, and 5 years, respectively. Those who survived to 1 year had a conditional median survival of 7.9 years.

A study, published by Shuhaiber et al in 2008, involved a review of data from the United Network for Organ Sharing (UNOS) registry.[18] The authors identified 799 primary heart-lung and 19 repeat heart-lung transplants. According to Kaplan-Meier survival analysis, the observed median survival times were 2.08 years after primary transplant and 0.34 years after repeat transplants. In addition, the authors analyzed survival data in matched pairs of primary and repeat transplant patients, who were matched on a number of potentially confounding demographic and clinical characteristics. Matches were not available for 4 repeat transplant patients. For the 15 repeat transplant patients with primary transplant matches, survival time did not differ significantly in the 2 groups. Being on a ventilator was statistically significantly associated with decreased survival time. The main limitation of this analysis is the small number of repeat transplant procedures performed.

Section Summary: Heart-lung Retransplantation
Analysis has suggested that patients undergoing heart/lung retransplantation have a lower median survival compared with patients undergoing primary heart/lung transplantation. However, after controlling confounding variables, survival times did not differ significantly between groups. Also, the conditional mean survival of 7.9 years among those who survived to 1-year posttransplant would suggest a survival benefit of heart/lung retransplant.

Potential Contraindications to Heart-lung Transplant (Applies to All Indications)
Individual transplant centers may differ in their guidelines, and individual patient characteristics may vary within a specific condition. In general, heart transplantation is contraindicated in

patients who are not expected to survive the procedure, or in whom patient-oriented outcomes, such as morbidity or mortality, are not expected to change due to comorbid conditions unaffected by transplantation (e.g., imminently terminal cancer or other disease). Further, consideration is given to conditions in which the necessary immunosuppression would lead to hastened demise (e.g., active untreated infection).However, stable chronic infections have not always been shown to reduce life expectancy in heart transplant patients.

Malignancy
Pretransplant malignancy is considered a relative contraindication for heart transplantation considering this has the potential to reduce life expectancy and could prohibit immune suppression after transplantation. However, with improved cancer survival over the years and use of cardiotoxic chemotherapy and radiotherapy, the need for heart transplantation has increased in this population.

Mistiaen et al (2015) conducted a systematic review to study the post-transplant outcome of pretransplant malignancy patients. Most selected studies were small case series (median sample size, 17 patients; range, 7-1117 patients).[19] Mean patient age varied from 6 to 52 years. Hematologic malignancy and breast cancer were the most common type of pretransplant malignancies. Dilated, congestive, or idiopathic cardiomyopathy was mostly the common reason for transplantation in 4 case series, chemotherapy related cardiomyopathy was the most important reason for transplantation in the other series. Hospital mortality varied between 0% and 33%, with small sample size potentially explaining the observed variation,

One large series reported similar short-term and long-term post-transplant survival of chemotherapy related (N=232) and other nonischemic cardiomyopathy (N=8890) patients.[20] The 1-, 3-, and 5-year survival rates of were 86%, 79%, and 71% for patients with chemotherapy-related cardiomyopathy compared with 87%, 81%, and 74% for other transplant patients. Similar findings were observed for 1-year survival in smaller series. Two-, 5-, and 10-year survival rates among pretransplant malignancy patients were also comparable with other transplant patients. In addition to the nonmalignancy related factors such as cardiac, pulmonary, and renal dysfunction, 2 malignancy related factors were identified as independent predictors of 5-year survival. Malignancy-free interval (the interval between treatment of cancer and heart transplantation) of less than 1 year was associated with lower 5-year survival compared with a longer interval (<60% vs. >75%).

Patients with prior hematologic malignancies had an increased post-transplant mortality in 3 small series. Recurrence of malignancy was more frequent among patients with a shorter disease-free interval, 63%, 26%, and 6% among patients with less than 1 year, 1 to 5 years, and more than 5 years of disease-free interval, respectively.[21]

Yoosabai et al (2015) conducted a retrospective review among 23,171 heart transplant recipient in the OPTN/UNOS database to identify whether pretransplant malignancy increases the risk of post-transplant malignancy.[22] Post transplant malignancy was diagnosed in 2673 (11.5%) recipients during the study period. A history of any pretransplant malignancy was associated with increased risk of overall post-transplant malignancy (subhazard ratio [SHR], 1.51; p<0.01), skin (SHR=1.55, p<0.01), and solid organ malignancies (SHR=1.54, p<0.01) on multivariate analysis.

Recurrence Risk
The evaluation of a candidate who has a history of cancer must consider the prognosis and risk of recurrence from available information including tumor type and stage, response to therapy, and time since therapy was completed. Although evidence is limited, patients in whom cancer is thought to be cured should not be excluded from consideration for transplant. The International Society for Heart & Lung Transplantation (ISHLT) guidelines have recommended to stratify each patient with pretransplant malignancy as to their risk of tumor recurrence and that cardiac transplantation should be considered when tumor recurrence is low based on tumor type, response to therapy and negative metastatic workup. The guidelines also recommended that the specific amount of time to wait to transplant after neoplasm remission will depend on these factors and no arbitrary time period for observation should be used.

Human Immunodeficiency Virus Infection (HIV)
Koval et al (2019) conducted a retrospective study to assess outcomes among 29 HIV-infected patients who underwent thoracic transplant at 14 sites in the U.S. and Europe.[23] Of the 29 patients, 21 received heart transplants, 7 received lung transplants, and 1 received heart-lung transplant. At the time of transplantation, 2 patients had detectable HIV RNA levels and the remainder were undetectable. All patients were on a 3-drug antiretroviral regimen at the time of transplantation. One year survival did not differ for patients with HIV who received heart (90%) and lung (86%) transplants compared to control patients without HIV (p=0.947 and 0.949, respectively) from the ISHLT database. Three and 5-year survival rates among patients with HIV were 73% and 64%, respectively for heart transplants, and 80% and 75%, respectively for lung transplants. Acute cellular rejection occurred in 14 (67%) heart transplant patients and 2 lung transplant patients. Infections were reported in 8 (39%) heart transplant patients and 7 (86%) lung transplant patients. Six patients (5 heart transplant and 1 lung transplant) developed malignancy; none were AIDS-defining malignancies. Suppression of HIV RNA continued for at least 1 year for all patients. One patient who had a detectable viral load at the time of (heart) transplant died after 3 years from AIDS-related complications and graft failure. However, this was due to lack of adherence and lack of appropriate follow-up. The second patient with a detectable viral load at the time of transplant lived for 10 years post-transplant. There are few data directly comparing outcomes for patients with and without HIV or for combined heart-lung transplants.

Current OPTN policy permits HIV-positive transplant candidates.[7]

The British HIV Association and the British Transplantation Society (2017) updated their guidelines on kidney transplantation in patients with HIV disease.[24] These criteria may be extrapolated to other organs:

- Adherent with treatment, particularly antiretroviral therapy
- Cluster of differentiation 4 count greater than 100 cells/mL (ideally >200 cells/mL) for at least 3 months
- Undetectable HIV viremia (<50 HIV-1 RNA copies/ml) for at least 6 months
- No opportunistic infections for at least 6 months
- No history of progressive multifocal leukoencephalopathy, chronic intestinal cryptosporidiosis, or lymphoma.

Other Potential Contraindications
Considerations for heart transplantation and lung transplantation alone may also pertain to combined heart-lung transplantation. For example, cystic fibrosis accounts for most pediatric

candidates for heart-lung transplantation, and infection with *Burkholderia* species is associated with higher mortality in these patients.

SUMMARY OF EVIDENCE

For individuals who have end-stage cardiac and pulmonary disease who receive combined heart-lung transplant, the evidence includes case series and registry data. Relevant outcomes include overall survival, symptoms, morbid events, and treatment-related morbidity and mortality. The available literature, consisting of case series and registry data, describes outcomes after heart-lung transplantation. Given the exceedingly poor expected survival without transplantation, this evidence is sufficient to demonstrate that heart-lung transplantation provides a survival benefit in appropriately selected patients. It may be the only option for some patients with end-stage cardiopulmonary disease. Heart-lung transplant is contraindicated 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. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have a prior combined heart-lung transplant subsequently undergoing graft failure or severe dysfunction of heart and lung who receive heart-lung transplant, the evidence includes case series and registry data. Relevant outcomes are overall survival, symptoms, morbid events, and treatment-related morbidity and mortality. A very limited amount of data has suggested that, after controlling for confounding variables, survival rates after primary and repeat heart-lung transplants is similar. Findings are not conclusive due to the small number of cases of repeat heart-lung transplants reported in the published literature. Repeat heart-lung transplantation is likely to improve outcomes in patients with a failed prior transplant who meet the clinical criteria for heart-lung transplantation. Given the small population of patients eligible for a heart-lung transplant, the evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

International Society for Heart and Lung Transplantation

The International Society for Heart and Lung Transplantation (2021) updated its consensus-based guidelines on the selection of lung transplant recipients.[25]

These guidelines made the following statements about lung transplantation:
“Lung transplantation should be considered for adults with chronic, end-stage lung disease who meet all the following general criteria:

- “High (>50%) risk of death from lung disease within 2 years if lung transplantation is not performed.
- High (>80%) likelihood of 5-year post-transplant survival from a general medical perspective provided that there is adequate graft function.”

For combined heart-lung transplant, the guidelines state:
"Candidates should meet the criteria for lung transplant listing and have significant dysfunction of one or more additional organs, or meet the listing criteria for a non-pulmonary organ transplant and have significant pulmonary dysfunction." The guideline goes on to state: "The

primary indication for heart-lung transplant is pulmonary hypertension, either secondary to idiopathic pulmonary arterial hypertension or congenital heart disease (CHD)."

"..candidates free from complex CHD or left ventricular compromise can achieve comparable outcomes with isolated bilateral lung transplant. Similarly, patients with advanced lung disease and cardiac pathology amenable to surgical repair may be candidates for lung transplant concurrent with the appropriate corrective cardiac procedure."

U.S. Preventive Services Task Force Recommendations
Not applicable.

ONGOING AND UNPUBLISHED CLINICAL TRIALS
A search of ClinicalTrials.gov did not identify any ongoing or unpublished trials that would likely influence this review.

Government Regulations

National:

There is no national coverage determination.

Heart-lung transplantation is covered under Medicare when performed in a facility that is approved by Medicare as meeting institutional coverage criteria.[28] The Centers for Medicare and Medicaid Services (CMS) has stated that under certain limited cases, exceptions to the criteria may be warranted if there is justification and if the facility ensures safety and efficacy objectives.

Local:

There is no local coverage determination.

(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 [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Transplant-Heart
- Transplant-Lung-Lobar Lung
- Transplant-Heart-Lung (Combined)
- Transplant-Heart-Kidney (Combined)
- Transplant-Islet Cell
- Transplant-Liver
- Transplant-Pancreas
- Transplant-Small Bowel-Liver/Multivisceral (Combined)
- Transplant-Small Bowel (Isolated)

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through January 2025, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
4/24/02	4/24/02	4/24/02	Joint policy established
12/5/03	12/5/03	1/16/04	Routine maintenance
2/15/05	2/15/05	2/2/05	Routine maintenance
9/1/06	7/10/10	7/5/06	Routine maintenance
9/1/07	7/3/07	7/11/07	Routine maintenance
11/1/08	8/19/08	10/30/08	Routine maintenance
3/1/10	12/8/09	12/8/09	Routine maintenance
9/1/12	6/12/12	6/19/12	Routine maintenance; policy reformatted to mirror BCBSA policy
11/1/13	8/22/13	8/27/13	Routine maintenance; references and rationale updated.
5/1/15	2/17/15	2/27/15	Routine maintenance – References and rationale updated; added statement to inclusions regarding retransplantation.
5/1/16	2/16/16	2/16/16	Routine maintenance-references, rationale, inclusion criteria and professional statements updated.
5/1/17	2/21/17	2/21/17	Routine policy maintenance.
5/1/18	2/20/18	2/20/18	Updated rationale, added reference # 1, 4, 12-15, 18-22 and 24. No change in policy status.
5/1/19	2/19/19		Routine policy maintenance. No change in policy status.
5/1/20	2/18/20		Routine policy maintenance. Inclusion/exclusion sections reorganized to match other transplant policies for consistency. No change in policy status.
5/1/21	2/16/21		Updated rationale, added references # 12, 15 and 24. No change in policy status.

5/1/22	2/15/22		Routine policy maintenance, no change in policy status.
5/1/23	2/21/23		Routine policy maintenance, “patients” replaced with “individuals” in MPS. No change in policy status. (ds)
5/1/24	3/8/24		Reworded MPS, no change in intent. Routine policy maintenance, no change policy status. Title change to Transplant: Heart-Lung (Combined). Vendor managed: N/A (ds)
5/1/25	2/18/25		Language changes in MPS, language added to inclusion section, rationale updated, reference #11 added. No change in status. Vendor managed: N/A (ds)

Next Review Date: 1st Qtr. 2026

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: TRANSPLANT-HEART-LUNG (COMBINED)

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered, policy guidelines 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.

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.