Policy Number	**SUR703.006**
Policy Effective Date	**11/15/2025**

Heart/Lung Transplant

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Related Policies (if applicable)
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Disclaimer

Carefully check state regulations and/or the member contract.
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For Texas ONLY: For policies (IFM, Student, Small Group, Mid-Market, Large Group, fully-insured Municipalities/Counties/Schools, State Employee Plans, PPO, HMO, POS) delivered, issued for delivery, or renewed on or after January 1, 2024, TIC Chapter 1380 (§§ 1380.001 – 1380.003 [SB 1040 Human Organ Transplant]) prohibits coverage of a human organ transplant or post-transplant care if the transplant operation is performed in China or another country known to have participated in forced organ harvesting; or the human organ to be transplanted was procured by a sale or donation originating in China or another country known to have participated in forced organ harvesting. The commissioner of state health services may designate countries who are known to have participated in forced organ harvesting. Forced organ harvesting is defined as the removal of one or more organs from a living person by means of coercion, abduction, deception, fraud, or abuse of power or a position of vulnerability.

Coverage

Heart/lung transplantation **may be considered medically necessary** for carefully selected individuals with end-stage cardiac and pulmonary disease including, but not limited to, one of the following diagnoses:

- 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 medically necessary** in individuals who meet criteria for heart/lung transplantation.

Heart/lung transplantation **is considered experimental, investigational and/or unproven** in all other situations.

Policy Guidelines

NOTE 1: For heart transplantation only, see policy SUR703.005, Heart Transplant.

NOTE 2: Refer to SUR703.001, Organ and Tissue Transplantation for general donor and recipient information.

NOTE 3: Refer to SUR703.010 Lung and Lobar Lung Transplant for ex vivo lung perfusion systems.

General Criteria
The factors below are potential contraindications subject to the judgment of the transplant center:

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

Heart/Lung-Specific Criteria
When the candidate is eligible to receive a heart in accordance with United Network for Organ Sharing (UNOS) guidelines for cardiac transplantation, the lung(s) shall be allocated to the heart/lung candidate from the same donor. When the candidate is eligible to receive a lung in accordance with the UNOS Lung Allocation System, the heart shall be allocated to the heart/lung candidate from the same donor "after the heart has been offered to all heart and

heart-lung potential transplant recipients in allocation classifications 1 through 4." Candidates with allocation classifications 1 through 4 fall within adult status 1 or 2 or pediatric status 1A.

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. Donor thoracic organs are prioritized by UNOS on the basis of recipient medical urgency, distance from donor hospital, and pediatric status. Individuals who are most severely ill (status 1A) are given highest priority.

The following factors are considered in assessing the severity of cardiac illness: reliance on continuous mechanical ventilation, infusion of intravenous inotropes, and/or dependency on mechanical circulatory support (i.e., total artificial heart, intra-aortic balloon pump, extracorporeal membrane oxygenator, ventricular assist device). Factors considered in assessing the severity of pulmonary illness include increased pulmonary artery systolic pressure, pulmonary arterial hypertension, and/or elevated pulmonary vascular resistance.

Additional criteria may be considered in pediatric individuals, including diagnosis of an OPTN-approved congenital heart disease diagnosis, presence of ductal dependent pulmonary or systemic circulation, and diagnosis of hypertrophic or restrictive cardiomyopathy while less than 1-year-old. Of note, pediatric heart transplant candidates who remain on the waiting list at the time of their 18th birthday without receiving a transplant continue to qualify for medical urgency status based on the pediatric criteria.

In both adult and pediatric individuals, isolated cardiac or pulmonary transplantations are preferred to combined heart/lung transplantation when medical or surgical management-other than organ transplantation-is available.

Full OPTN guidelines are available online at <https://optn.transplant.hrsa.gov>.

Individuals who are considered temporarily unsuitable to receive a thoracic organ transplant may be assigned an inactive status.

Description

Heart/lung transplantation involves a coordinated triple operative procedure consisting of procurement of a donor heart/lung block, excision of the heart and lungs of the recipient, and implantation of the heart and lungs into the recipient. Heart/lung transplantation refers to the transplantation of 1 or both lungs and heart from a single cadaver donor.

Background
Solid organ transplantation offers a treatment option for individuals with different types of end-stage organ failure that can be lifesaving or provide significant improvements to a patient's quality of life. (1) 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 (OPTN) and United Network of Organ Sharing (UNOS).

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. (2)

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. (3)

In 2024, 48,149 transplants were performed in the United States (U.S.) procured from more than 41,000 deceased donors and 7000 living donors. (4) Of these transplants, 64 individuals received heart/lung transplants in the U.S. in 2024 (total 1610 heart-lung transplants done to date in the U.S.). As of July 2025, 50 patients were on the waiting list for heart/lung transplants.

<u>Prioritization of Candidates</u>

Patients who are eligible for heart/lung transplantation can be listed under both the heart and lung allocation systems in the U.S. In 2005, UNOS changed the method by which lungs were allocated, from 1 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 the likelihood of survival. (5) 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 with pulmonary hypertension who meet the following criteria (6):

- Deterioration of optimal therapy, and
- Right arterial pressure greater than 15 mm Hg, or
- Cardiac index less than 1.8 L/min/m^2.

Specific criteria for prioritizing donor thoracic organs for transplant are provided by the OPTN and implemented through a contract with UNOS. (7)

Yusen et al. (2016) analyzed data on heart/lung transplantations performed among adults between 1982 and 2015 using the registry of the International Society for Heart and Lung Transplantation (ISHLT). (3) Among the 3397 heart/lung transplant recipients for whom the diagnosis was reported, 35% had congenital heart disease (CHD), 27% had pulmonary arterial hypertension, and 14% had cystic fibrosis as the primary indication. There has been a shift in indications for heart/lung transplantation over time. From 2004 to 2015, CHD (35%), pulmonary arterial hypertension (27%), and cardiomyopathy (11%) were the 3 most common indications for heart/lung transplantation. Of the 883 heart/lung transplant recipients between 2004 and 2015, 36% were 18 to 34 years old, 40% were 35 to 49 years old, 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. (8) 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 alpha$_1$-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. (9) 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 a non-cytomegalovirus 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. (10)

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 (FDA).

The FDA 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.

Rationale

Medical policies assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the 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 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 technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 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 (RCT) 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 RCTs comparing heart/lung transplant with alternatives. Systematic reviews are based on case series and registry data. Randomized controlled trials compare surgical technique, infection prophylaxis, and immunosuppressive therapy and are not germane to this medical policy.

Initial Combined Heart/Lung Transplant

Clinical Context and Therapy Purpose

The purpose of combined heart/lung transplant in individuals who have an 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 PICO was used to select literature to inform this policy.

Populations

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

Interventions

The therapy being considered is a 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.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Systematic Review
Yan et al. (2023) conducted a systematic review comparing outcomes between bilateral lung transplantation and heart-lung transplantation. (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% confidence interval [CI], 1.00 to 1.11; p=.06), 3 years (RR, 1.06; 95% CI, 0.98 to 1.15; p=.13), 5 years (RR, 1.02; 95% CI, 0.92 to 1.13; p=0.71), or 10 years (RR, 1.03; 95% CI, 0.90 to 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 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=.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=.7).

Yusen et al. (2016) reported on the survival of adult heart/lung transplant recipients using the International Society for Heart and Lung Transplantation (ISHLT) database. (3) Among the 3775 primary heart/lung transplants performed between 1982 and 2014, the 3-month, 1-year, 3-

year, 5-year, and 10-year survival rates were 71%, 63%, 52%, 45%, and 32%, respectively. The overall median survival during this period (1982 to 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 a median survival of 2.1 years for patients (n=1596) who received the transplant between 1982 and 1993, 3.9 years for patients (n=1392) between 1994 and 2003, and 5.8 years for patients between 2004 and 2014 (n=843) (p<.05 for all pairwise 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 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 among adult transplant recipients in the Scientific Registry of Transplant Recipients database between 1987 and 2012. (13) Among the 928 idiopathic pulmonary arterial hypertension 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 hospitalized in the intensive care unit, double-lung transplantation was associated with worse outcomes than heart/lung transplantation recipients (hazard ratio [HR], 1.83; 95% CI, 1.02 to 3.28).

Jayarajan et al. (2014) compared the mortality rates (at 1 month and 5 years posttransplant) of heart/lung transplant recipients who required pretransplant ventilation (n=22) or extracorporeal membrane oxygenation (ECMO; n=15) with controls. (14) Median survival times were 10 days, 181 days, and 1547 days among patients with pretransplant ECMO, patients with a mechanical ventilator, and the control group, respectively. Patients with pretransplant ECMO had poorer survival than the control group at 30 days (20.0% vs 83.5%) and 5 years (20.0% vs 47.4%; p<.001). Similarly, patients requiring ventilation prior to transplantation had worse survival at 1 month (77.3% vs 83.5%) and 5 years (26.5% vs 47.4%; p<.001) compared with the control group. The use of ECMO (HR, 3.82; 95% CI, 1.60 to 9.12; p=.003) or mechanical ventilation (HR, 2.01; 95% CI, 1.07 to 3.78; p=.030) as a bridge to transplantation was independently associated with mortality on multivariate analysis. The findings of the study raise concern whether combined heart/lung transplant should be carried out in patients requiring ECMO; further, the findings suggest a need for additional 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=.03) and patients who were retransplanted (p=.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=.04), patients 1 to 11 years of age (HR, 1.78; 95% CI, 1.12 to 2.8; p=.015), and patients on ECMO (HR, 4.1; 95% CI, 1.3 to 12.8; p=.016) had the highest risk of mortality post-transplant.

Goldfarb et al. (2016) reported on 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 time period of transplant for pediatric heart/lung transplant recipients.

Section Summary: Initial Heart/Lung Transplant

Data from transplantation registries have found longer patient survival rates after initial heart/lung transplant among adult and pediatric patients over time. The net benefit of heart transplantation compared with 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 retransplants 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 PICO was used to select literature to inform this policy.

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 a 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.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Registry Studies
While uncommon, repeat heart/lung transplant procedures have been performed. Yusen et al. (2014) reported on 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 years, with unadjusted survival rates 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 by Shuhaiber et al. (2008) reviewed data from the UNOS registry. (18) They identified 799 primary heart/lung transplants and 19 repeat heart/lung transplants. Using Kaplan-Meier survival analysis, the observed median survival times were 2.08 years after the primary transplant and 0.34 years after repeat transplant. In addition, reviewers 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 between groups. Being on a ventilator was statistically significantly associated with decreased survival time. The main limitation of this analysis was the low 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 (e.g., morbidity, mortality) are not expected to change due to comorbid conditions unaffected by transplantation (e.g., imminently terminal cancer, or another 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 given that malignancy has the potential to reduce life expectancy and could prohibit immune suppression after transplantation. However, with improved cancer survival and the 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 posttransplant outcomes for pretransplant malignancy patients. Most selected studies were small case series (median sample size, 17 patients; range, 7 to 1117 patients; mean age, 6 to 52 years). (19) Hematologic malignancy and breast cancer were the most common types of pretransplant malignancies. Dilated, congestive, or idiopathic cardiomyopathy were the most common reasons for transplantation in 4 case series; chemotherapy-related cardiomyopathy was the most important reason for transplantation in the other series. Hospital mortality rates ranged between 0% and 33%, with small sample sizes potentially explaining the observed variation.

A large series by Oliveira et al. (2012) reported similar short- and long-term posttransplant survival rates for chemotherapy-related (n=232) and other nonischemic cardiomyopathy (n=8890) patients. (20) The 1-, 3-, and 5-year survival rates were 86%, 79%, and 71% for patients with chemotherapy-related cardiomyopathy compared with 87%, 81%, and 74% for other transplant patients, respectively. Further, 2-, 5-, and 10-year survival rates among pretransplant malignancy patients were found to be comparable with other transplant patients. In addition to the non-malignancy-related factors such as cardiac, pulmonary, and renal dysfunction, 2 malignancy-related factors were identified as independent predictors of 5-year survival. A malignancy-free interval (the interval between treatment of cancer and heart transplantation) of less than 1 year was associated with lower 5-year survival (<60%) than with a longer interval (>75%).

Patients with prior hematologic malignancies had increased posttransplant mortality in 3 small series. For example, as reported by Sigurdardottir et al. (2012), 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 of 23,171 heart transplant recipients in the Organ Procurement and Transplantation Network (OPTN)/UNOS database to identify whether pretransplant malignancy increased the risk of posttransplant malignancy. (22) Posttransplant malignancy was diagnosed in 2673 (11.5%) recipients during the study period. A history of any pretransplant malignancy was associated with an increased risk of overall posttransplant malignancy (subhazard ratio, 1.51; p<.01), skin malignancies (subhazard ratio, 1.55; p<.01), and solid organ malignancies (subhazard ratio, 1.54; p<.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 ISHLT guidelines have recommended stratifying 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 for transplant after neoplasm remission will depend on these factors and no arbitrary time period for observation should be used.

Human Immunodeficiency Virus (HIV) Infection

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 a 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=.947 and p=.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 a systematic review, case series, and registry data. Relevant outcomes are overall survival, symptoms, morbid events, and treatment-related morbidity and mortality. The available literature reports on outcomes after heart/lung transplantation. Given the exceedingly poor expected survival rates without transplantation, this evidence is sufficient to demonstrate that heart/lung transplantation provides a survival benefit in appropriately selected patients. A transplant may be the only option for some patients with end-stage cardiopulmonary disease. Heart/lung transplant is contraindicated for patients in whom the procedure is expected to be futile due to comorbid disease or for whom post-transplantation care is expected to worsen comorbid conditions significantly. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have a combined heart/lung transplant complicated by graft failure or severe dysfunction of the heart/lung and who receive a combined heart/lung retransplant, 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 are similar. Findings are inconclusive due to the small number of cases of repeat heart/lung transplants reported in the published literature. Repeat heart/lung transplantation is, however, likely to improve outcomes in patients with a prior failed transplant who meet the clinical criteria for heart/lung transplantation. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements

American Thoracic Society

In 2025, the American Thoracic Society published guidelines on interventional strategies for children with progressive pulmonary hypertension (PH). (25) Regarding combined heart and lung transplantation for PH, the guideline states this should be reserved for the "rare situations of uncorrectable congenital heart disease, coexisting left ventricular dysfunction, and technical issues such as massive right heart enlargement in young children, donor lung constraints, and lower likelihood of airway caliber compromise with tracheal versus bibronchial anastomoses in small children (as the child grows)."

International Society for Heart and Lung Transplantation

In 2021, the International Society for Heart and Lung Transplantation (ISHLT) updated its consensus-based guidelines on the selection of lung transplant recipients. (26) 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)."

The guidelines also mentioned: "...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."

In 2024, ISHLT updated its guidelines for the evaluation and care of cardiac transplant candidates. (27) Recommendations for combined heart/lung transplantation include the following:

- "In heart transplant candidates deemed ineligible for transplantation due to severe irreversible end-stage parenchymal lung disease, evaluation for combined heart and lung transplantation may be considered (class of recommendation [COR], 2b [weak]; level of evidence [LOE], consensus of expert opinion based on clinical experience [C-EO])."
- "In heart transplant candidates deemed ineligible for transplantation due to severe irreversible PH, evaluation for combined heart and lung transplantation may be considered in carefully selected patients (COR, 2b; LOE, C-EO)."

Medicare National Coverage

Heart/lung transplantation is covered under Medicare when performed in a facility approved by Medicare as meeting institutional coverage criteria. (28) The Centers for Medicare & Medicaid Services 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.

Ongoing and Unpublished Clinical Trials

A search of ClinicalTrials.gov in July 2025 did not identify any ongoing or unpublished trials that would likely influence this policy.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	33930, 33933, 33935, 33946, 33947, 33948, 33949, 0494T, 0495T, 0496T
HCPCS Codes	S2152

References

1. Black CK, Termanini KM, Aguirre O, et al. Solid organ transplantation in the 21st century. Ann Transl Med. Oct 2018; 6(20):409. PMID 30498736
2. Christie JD, Edwards LB, Kucheryavaya AY, et al. The Registry of the International Society for Heart and Lung Transplantation: twenty-seventh official adult lung and heart-lung transplant report--2010. J Heart Lung Transplant. Oct 2010; 29(10):1104-1118. PMID 20870165
3. Yusen RD, Edwards LB, Dipchand Al, et al. The Registry of the International Society for Heart and Lung Transplantation: Thirty-third Adult Lung and Heart-Lung Transplant Report-2016; Focus Theme: Primary Diagnostic Indications for Transplant. J Heart Lung Transplant. Oct 2016; 35(10):1170-1184. PMID 27772669
4. United Network for Organ Sharing (UNOS). Transplant trends. 2025. Available at <https://unos.org> (accessed July 29, 2025).
5. Kalogeropoulos AP, Georgiopoulou VV, Giamouzis G, et al. Utility of the Seattle Heart Failure Model in patients with advanced heart failure. J Am Coll Cardiol. Jan 27 2009; 53(4):334-342. PMID 19161882

6. United Network for Organ Sharing (UNOS). Lung CAS summary data updated. 2024. Available at <https://www.unos.org> (accessed July 30, 2025).
7. Organ Procurement and Transplantation Network (OPTN). Organ Procurement and Transplantation Network Policies. Updated June 26, 2025. Available at <https://optn.transplant.hrsa.gov> (accessed July 30, 2025).
8. Spahr JE, West SC. Heart-lung transplantation: pediatric indications and outcomes. J Thorac Dis. Aug 2014; 6(8):1129-1137. PMID 25132980
9. Benden C, Edwards LB, Kucheryavaya AY, et al. The registry of the international society for heart and lung transplantation: fifteenth pediatric lung and heart-lung transplantation report-2012. J Heart Lung Transplant. Oct 2012; 31(10):1087-1095. PMID 22975098
10. Benden C, Goldfarb SB, Edwards LB, et al. The registry of the International Society for Heart and Lung Transplantation: seventeenth official pediatric lung and heart-lung transplantation report--2014; focus theme: retransplantation. J Heart Lung Transplant. Oct 2014; 33(10):1025-1033. PMID 25242126
11. Yan HJ, Zheng XY, Huang H, et al. Double-lung versus heart-lung transplantation for end-stage cardiopulmonary disease: a systematic review and meta-analysis. Surg Today. Sep 2023; 53(9):1001-1012. PMID 36068414
12. Sertic F, Han J, Diagne D, et al. Not all septal defects are equal: outcomes of bilateral lung transplant with cardiac defect repair vs combined heart-lung transplant in patients with Eisenmenger syndrome in the United States. Chest. Nov 2020; 158(5):2097-2106. PMID 32565271
13. Hill C, Maxwell B, Boulate D, et al. Heart-lung vs. double-lung transplantation for idiopathic pulmonary arterial hypertension. Clin Transplant. Dec 2015; 29(12):1067-1075. PMID 26358537
14. Jayarajan SN, Taghavi S, Komaroff E, et al. Impact of extracorporeal membrane oxygenation or mechanical ventilation as bridge to combined heart-lung transplantation on short-term and long-term survival. Transplantation. Jan 15 2014; 97(1):111-115. PMID 24056630
15. Riggs KW, Chapman JL, Schecter M, et al. Pediatric heart-lung transplantation: A contemporary analysis of outcomes. Pediatr Transplant. May 2020; 24(3):e13682. PMID 32067330
16. Goldfarb SB, Levvey BJ, Edwards LB, et al. The Registry of the International Society for Heart and Lung Transplantation: Nineteenth Pediatric Lung and Heart-Lung Transplantation Report-2016; Focus Theme: Primary Diagnostic Indications for Transplant. J Heart Lung Transplant. Oct 2016; 35(10):1196-1205. PMID 27772671
17. Yusen RD, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-first adult lung and heart-lung transplant report--2014; focus theme: retransplantation. J Heart Lung Transplant. Oct 2014; 33(10):1009-1024. PMID 25242125
18. Shuhaiber JH, Kim JB, Gibbons RD. Repeat heart-lung transplantation outcome in the United States. J Heart Lung Transplant. Oct 2008; 27(10):1122-1127. PMID 18926404
19. Mistiaen WP. Heart transplantation in patients with previous malignancy. An overview. Acta Cardiol. Apr 2015; 70(2):123-130. PMID 26148371

20. Oliveira GH, Hardaway BW, Kucheryavaya AY, et al. Characteristics and survival of patients with chemotherapy- induced cardiomyopathy undergoing heart transplantation. J Heart Lung Transplant. Aug 2012; 31(8):805-810. PMID 22551930
21. Sigurdardottir V, Bjortuft O, Eiskjaer H, et al. Long-term follow-up of lung and heart transplant recipients with pre- transplant malignancies. J Heart Lung Transplant. Dec 2012; 31(12):1276-1280. PMID 23089300
22. Yoosabai A, Mehta A, Kang W, et al. Pretransplant malignancy as a risk factor for posttransplant malignancy after heart transplantation. Transplantation. Feb 2015; 99(2):345-350. PMID 25606783
23. Koval CE, Farr M, Krisl J, et al. Heart or lung transplant outcomes in HIV-infected recipients. J Heart Lung Transplant. Dec 2019; 38(12):1296-1305. PMID 31636044
24. Working Party of the British Transplantation Society. Kidney and Pancreas Transplantation in Patients with HIV. Second Edition (Revised). British Transplantation Society Guidelines. Macclesfield, UK: British Transplantation Society; Published 2015. Updated 2017. Available at <https://www.bts.org.uk> (accessed July 30, 2025).
25. Hayes D, Jennerich AL, Coleman RD, et al. Interventional Strategies for Children with Progressive Pulmonary Hypertension Despite Optimal Therapy: An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med. Feb 2025; 211(2):157-173. PMID 39531626
26. Leard LE, Holm AM, Valapour M, et al. Consensus document for the selection of lung transplant candidates: An update from the International Society for Heart and Lung Transplantation. J Heart Lung Transplant. Nov 2021; 40(11):1349-1379. PMID 34419372
27. Peled Y, Ducharme A, Kittleson M, et al. International Society for Heart and Lung Transplantation Guidelines for the Evaluation and Care of Cardiac Transplant Candidates-2024. J Heart Lung Transplant. Oct 2024; 43(10):1529-1628.e54. PMID 39115488
28. Center for Medicare and Medicaid Services (CMS). Decision Memo for TRANSPLANT Centers: Re-Evaluation of Criteria for Medicare Approval (CAG-00061N). 2000. Available at <https://www.cms.gov> (accessed July 30, 2025).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been changed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change

11/15/2025	Document updated. Coverage unchanged. Added references 25 and 27; others updated.
10/15/2024	Document updated with literature review. Coverage unchanged. Added reference 11; others updated.
02/01/2024	Document updated with literature review. Coverage unchanged. Added reference 24; others updated.
10/15/2022	Reviewed. No changes.
07/15/2021	Document updated with literature review. Coverage unchanged. Added/updated the following references: 1, 4, 6, 8, 12, 15, 23 and 27.
01/15/2021	Reviewed. No changes.
06/15/2020	Document updated with literature review. Coverage unchanged. Reference 4 added and some references removed.
11/15/2018	Reviewed. No changes.
12/15/2017	Document updated with literature review. Coverage unchanged.
03/15/2016	Reviewed. No changes.
06/01/2015	Document updated with literature review. Coverage unchanged.
12/01/2014	Document updated with literature review. The following statements were added to coverage: 1) Heart/lung retransplantation after a failed primary heart/lung transplant may be considered medically necessary in patients who meet criteria for heart/lung transplantation. 2) Heart/lung transplantation is considered experimental, investigational and/or unproven in all other situations. Title changed from: Heart and Lung Transplant.
11/01/2013	Document updated with literature review. The following criteria and statements were removed from Coverage: 1) Are free of active alcohol or narcotic abuse; 2) Can deal with the postoperative and the life-long medical regimen on a physical and psychological basis; 3) Are free of comorbid conditions such as active systemic infection and malignancy; 4) A heart-lung transplant is considered experimental, investigational and unproven in patients with active systemic illness or serious comorbidities that would be expected to have a substantial effect on successful completion or outcome of transplant surgery; 5) "NOTE: End-stage heart failure as confirmed by either New York Heart Association (NYHA) classification of Status III or IV patients; or peak oxygen consumption (VO2) > 15 ml/kg/min [milliliter/kilogram/minute] or 55% of predicted VO2; OR The American College of Cardiology (ACC) guidelines for Status II patients. See description." In addition, CPT/HCPCS code(s) updated.
04/15/2009	References revised; No change in coverage, remains conditional.
06/01/2008	Revised/updated entire document
02/01/2005	Revised/updated entire document
05/01/1996	Medical policy number changed
04/01/1996	Revised/updated entire document
01/01/1992	Revised/updated entire document

05/01/1990	New medical document