Overview

This Coverage Policy addresses transplantation of the thoracic organs (i.e., heart, lung), surgical procedures in which one or both of the diseased organs are replaced with the viable heart, lung(s), lung lobes, or combined heart and lung of an appropriate donor.

Coverage Policy

Heart transplantation in an adult is considered medically necessary for the treatment of ANY of the following:

- malignant ventricular arrhythmias unresponsive to medical and/or surgical therapy
- refractory angina that is not amenable or correctable by alternative medical or surgical therapies and leaves the individual in a New York Heart Association functional class III or IV
- end-stage heart failure with EITHER of the following:
  - disease that is not amenable or correctable by alternative medical therapies or leaves the individual in New York Heart Association functional class III or IV
  - disease that requires continuous intravenous inotropic or mechanical circulatory support

Heart transplantation in a child is considered medically necessary for the treatment of EITHER of the following:
• intractable heart failure
• congenital abnormality not amenable to surgical correction

Lung transplantation from a deceased donor is considered medically necessary when BOTH of the following criteria are met:

• end-stage disease of lung parenchyma, airway and pulmonary vasculature that is not amenable to maximum alternative medical or surgical therapies
• severe, progressive symptoms with a functional status of New York Heart Association class III or IV despite optimal medical management, resulting in an unacceptable quality of life

Heart-lung transplantation is considered medically necessary when BOTH of the following criteria are met:

• end-stage cardiopulmonary disease where the replacement of either organ alone is unlikely to improve survival or quality of life
• the individual remains at a New York Heart Association functional class III or IV despite maximal medical and surgical management

Note: Selected candidates may be eligible for multi-organ transplantation. In each case, the candidate should meet all of the criteria for selection for the individual transplant being considered.

Lung transplantation is considered experimental, investigational or unproven for EITHER of following:

• coronary artery disease not amenable to percutaneous intervention or bypass grafting, or associated with significant impairment of left ventricular function
• chest wall/spinal deformity that would pose a contraindication to transplantation

Ex vivo lung perfusion (e.g., Organ Care System™) for lung transplantation is considered experimental, investigational or unproven.

Heart, lung, or heart-lung transplantation is considered not medically necessary in an individual with ANY of the following contraindications to transplant surgery:

• malignancy that is expected to significantly limit future survival
• persistent, recurrent or unsuccessfully treated major or systemic infections
• systemic illness or comorbidities that would be expected to substantially negatively impact the successful completion and/or outcome of transplant surgery
• a pattern of demonstrated noncompliance which would place a transplanted organ at serious risk of failure
• human immunodeficiency virus (HIV) disease unless ALL of the following are noted:
  ➢ CD4 count greater than 200 cells/mm$^3$
  ➢ HIV-1 ribonucleic acid (RNA) undetectable
  ➢ stable anti-retroviral therapy for more than three months
  ➢ absence of serious complications associated with or secondary to HIV disease (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidioidomycosis; resistant fungal infections; or Kaposi’s sarcoma or other neoplasm)

**General Background**

**Heart Transplantation**
Heart transplantation is the therapy of choice in adults with end-stage heart failure, refractory angina, and malignant ventricular arrhythmias, who have received maximal medical treatment, are unlikely to survive the next
6–12 months and for whom there is no other surgical option (Mancini, 2019; Canter, et al., 2007; Butler, et al., 2004). According to the Organ Procurement and Transplantation Network (OPTN) Administrative Rules and Definitions policy, each heart transplant candidate is assigned a status that reflects the candidate’s medical urgency for transplant (OPTN, Jul 2019).

In 2019, the OPTN updated the adult heart allocation criteria for medical urgency status. The candidate must be at least 18 years old at the time of registration with the following requirements (OPTN, Jul 2019):

Adult Heart Status 1 requires that the patient has at least one of the following conditions:

- is supported by veno-arterial extracorporeal membrane oxygenation (VA ECMO)
- is supported by non-dischargeable, surgically implanted, non-endovascular biventricular support device
- is supported by mechanical circulatory support device (MCSD) with life-threatening ventricular arrhythmia

Adult Heart Status 2 requires that the patient has at least one of the following conditions:

- is supported by a non-dischargeable, surgically implanted, non-endovascular left ventricular assist device (LVAD)
- is supported by a total artificial heart (TAH), biventricular assist device (BiVAD), right ventricular assist device (RVAD), or ventricular assist device (VAD) for single ventricle patients
- is supported by a MCSD with device malfunction/mechanical failure
- is supported by a percutaneous endovascular mechanical circulatory support device
- is supported by an intra-aortic balloon pump (IABP)
- is experiencing recurrent or sustained ventricular tachycardia or ventricular fibrillation

Adult Heart Status 3 requires that the patient has at least one of the following conditions:

- is supported by a dischargeable left ventricular assist device and is exercising 30 days of discretionary time
- is supported by multiple inotropes or a single high dose inotrope and has hemodynamic monitoring
- is supported by VA ECMO after 7 days; percutaneous endovascular circulatory support device or IABP after 14 days
- is supported by non-dischargeable, surgically implanted, non-endovascular LVAD after 14 days
- is supported by an MCSD with one of the following:
  - hemolysis
  - pump thrombosis
  - device infection
  - mucosal bleeding
  - aortic insufficiency
  - right heart failure

Adult Heart Status 4 requires that the patient has at least one of the following conditions:

- is supported by dischargeable LVAD without discretionary 30 days
- is supported by inotropes without hemodynamic monitoring
- is a retransplant
- has a diagnosis of one of the following:
  - congenital heart disease (CHD)
  - ischemic heart disease with intractable angina
  - hypertrophic cardiomyopathy
  - restrictive cardiomyopathy
  - amyloidosis
Adult Heart Status 5 is for patients who are on the waitlist for at least one other organ at the same hospital and status 6 is for all remaining active candidates.

Justification for pediatric heart status 1A includes patients less than 18 years old at the time of registration with at least one of the following conditions:

- requires continuous mechanical ventilation or assistance of an intra-aortic balloon pump and is admitted to the hospital that registered the patient
- has ductal dependent pulmonary or systemic circulation, with ductal patency maintained by stent or prostaglandin infusion and is admitted to the hospital that registered the patient
- has a hemodynamically significant congenital heart disease diagnosis, requires infusion of multiple intravenous inotropes or a high dose of a single intravenous inotrope and is admitted to the hospital that registered the patient
- requires assistance of a mechanical circulatory support device

Requirements for pediatric heart status 1B includes at least one of the following criteria:

- requires infusion of one or more inotropic agents but does not qualify for pediatric status 1A
- younger than one year old at the time of the candidate’s initial registration and has a diagnosis of hypertrophic or restrictive cardiomyopathy

The OPTN’s national data for primary heart transplantation performed between 2008-2015 states that one-, three-, and five-year patient overall survival (OS) rates for primary transplantation were 90.9%, 85.5% and 78.6% respectively (based on OPTN data as of July 26, 2019). Risk factors for mortality after transplantation include retransplantation, intertransplant time (i.e., time between primary and retransplantation) of < 180 days, and the use of a total artificial heart as a bridge to transplant. Furthermore, the need for end-organ support with mechanical ventilation or dialysis, conferred the greatest risk of one-year mortality. Additional risk factors include the use of amiodarone pretransplantation, prior coronary artery bypass grafting (CABG) before transplantation, and transplantation of a female heart into a male recipient (Pham, 2019; Mahle, 2008; Canter, et al., 2007).

Indications for Heart Transplantation: An individual with refractory angina or end-stage intractable heart failure that is not amenable or correctable by alternative medical or surgical therapies and who has a New York heart Association (NYHA) III or IV functional class may be an appropriate candidate for heart transplantation. The New York Heart Association (NYHA) Functional Classification of Patients with Heart Disease is a subjective measure of functional capacity which describes the amount of activity an individual can do before the onset of heart failure symptoms is noted. Heart transplantation may also be indicated for an individual with malignant ventricular arrhythmias which are unresponsive to medical or surgical therapies.

In an infant or child, heart transplantation is indicated for end-stage cardiomyopathy when refractory to medical therapy, as well as previously repaired or palliated congenital heart disease when the individual has developed ventricular dysfunction or other nonoperable late-term complications. An infant or child with complex congenital heart disease (e.g., pulmonary atresia with intact septum and coronary arterial stenosis, some forms of hypoplastic left heart syndrome) for whom standard surgical procedures are extremely high risk may also be an appropriate candidate for heart transplantation (Bernstein, 2016).

Literature Review for Heart Transplantation: Heart transplantation is considered a standard of care for selected individuals. No prospective randomized study comparing heart transplantation to optimal medical therapy has been reported; however, several retrospective reviews and database analyses have demonstrated improved long-term outcomes with heart transplantation for selected individuals (Colvin, et al., 2018; Deuse, et al., 2008; Tjiang, et al., 2008; Weiss, et al., 2008).

Professional Societies/Organizations
American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA): The 2018 ACC/AHA guideline for the management of adults with congenital heart disease (ACHD) stated that cardiac transplantation is reasonable in adults with Fontan palliation with signs and symptoms of protein-losing enteropathy. Additionally, in patients with ACHD and Eisenmenger syndrome exhibiting
deteriorating functional ability, mechanical circulatory and pulmonary support, lung transplantation with concomitant repair of anatomic cardiovascular defects, and heart–lung transplantation have been applied (Stout, et al., 2019).

The 2013 ACC/AHA guideline for the management of heart failure (Yancy, et al., 2013) noted that heart transplantation is the gold standard for the treatment of refractory end-stage heart failure. Evaluation for cardiac transplantation is indicated for carefully selected patients with stage D heart failure despite guideline-directed medical therapy, device, and surgical management.

A 2011 ACC/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy (HCM) (Gersh, 2011) noted that patients with advanced (i.e., end-stage) heart failure and nonobstructive HCM not otherwise amenable to other treatment interventions with ejection fraction (EF) ≤ 50%, or occasionally with preserved EF, should be considered for heart transplantation. Symptomatic children with HCM with restrictive physiology who are not responsive to, or appropriate candidates for, other therapeutic interventions should be considered for heart transplantation. In general, indications for heart transplantation included advanced heart disease, typically with NYHA functional class III or IV symptoms that are refractory to all other reasonable interventions. Heart transplantation should not be performed in mildly symptomatic patients of any age with HCM.

American Heart Association (ASA): The 2016 AHA scientific statement on chronic heart failure in congenital heart disease stated that transplantation is a reasonable consideration in pediatric patients with heart failure associated with systemic ventricular dysfunction with previously repaired or palliated chronic heart disease (CHD) when it is associated with significant growth failure attributable to the heart disease and CHD with severe limitation of exercise and activity. Additional indications included: CHD with normal ventricular function if the following anatomic and physiological conditions are present and not amenable to surgical intervention (Stout, et al., 2016):

- proximal coronary arteries have severe stenosis or atresia
- atrioventricular or systemic semilunar valve(s) with moderate to severe stenosis or insufficiency
- symptomatic arterial oxygen desaturation (cyanosis)
- persistent protein-losing enteropathy despite optimal medical-surgical therapy

Lung Transplantation

Lung transplantation is the surgical replacement of the lung(s) of an individual with end-stage pulmonary disease with the partial (lobar) or whole lung or lungs of a living or deceased donor. For most recipients, lung transplantation is a palliative, rather than curative treatment, the primary goal being the projected survival benefit. It is an accepted treatment of last resort for persons with end-stage lung disease who do not respond to alternative medical or surgical treatment. Improvements in quality of life, in addition to survival, should be used to assess the effectiveness of the procedure (Orens, et al., 2006).

The type of lung transplantation procedure used (i.e., lobar, single, or double) and donor type (i.e., deceased or living) are based upon the candidate's condition and indication for transplantation, and the availability of donor organs. As donor organs are scarce relative to the number of candidates needing transplantation, conservation of acceptable donor organs is also taken into consideration.

Deceased Donor Lung Transplantation: A deceased donor, also known as cadaveric donor, is the most common donor source used for lung transplantation. The 2019 OPTN policy on the allocation of lungs stated that lung candidates < 12 years old are assigned a priority for lung allocation that is based on medical urgency and patients at least 12 years old are assigned a Lung Allocation Score (LAS) to determine lung allocation.

According to the Organ Procurement and Transplantation Network (OPTN) national data for deceased donor primary lung transplantation performed between 2008 and 2015, graft survival rates were 86.7%, 67.8% and 52.5%, respectively, at one-, three-, and five years (based on OPTN data as of July 26, 2019).

Living Donor Lung Transplantation (LDLT): Use of a live donor as a source for lung transplantation was initiated in 1993 due to the higher demand than supply for patients waiting for lung transplantation. Although
LDLT may be appropriate for a highly selected individual who likely would not survive waiting times for a deceased donor, it is now rarely performed. According to the 2017 OPTN annual report, only one living donor lung transplant (LDLT) was performed in 2012. In 2017 there were not any living donor lung transplants performed (OPTN/SRTR 2017 Annual Data Report: Lung). This procedure requires the donation of one lung lobe from each of two living donors. Major complications have included pleural effusion, bronchial stump fistula, bilobectomy, hemorrhage phrenic nerve injury, pulmonary artery thrombosis, and bronchial stricture. Minor complications include persistent air leak, arrhythmia, and pneumonia. Deceased donor transplantation is preferred to avoid the risk to two healthy donors (Solomon, et al., 2010).

**Indications for Lung Transplantation:** Lung transplantation should be considered for adults with chronic, end-stage lung disease, progressive symptoms, a New York Heart Association (NYHA) functional class III or IV that has not responded to medical or surgical therapies. There are four primary diagnostic groupings of lung disease for which transplantation may be indicated. Along with examples of each category, these include (Yusen, et al., 2016):

- chronic obstructive lung disease (COPD) (e.g., alpha-1 antitrypsin deficiency, non alpha-1 antitrypsin deficiency)
- interstitial lung disease (ILD) (e.g., idiopathic pulmonary fibrosis (IPF), idiopathic interstitial pneumonia [IIP])
- cystic fibrosis (e.g., bronchiectasis)
- pulmonary vascular disease (e.g., primary/idiopathic pulmonary hypertension, Eisenmenger syndrome)

Disease-specific parameters used to determine appropriateness for lung transplantation have been suggested by the International Society for Heart and Lung Transplantation (ISHLT) (Yusen, et al., 2016; Weill, et al., 2015; Orens, et al., 2006), the American Society of Transplantation (Faro, et al., 2007; Steinman, et al., 2001) and other published scientific literature (Kotloff, 2010; Lynch, et al., 2006) and include the following (Weill, et al., 2015):

**Chronic Obstructive Airway Disease:**
- BODE index (i.e., body mass index [B], degree of obstruction [O], dyspnea [D], exercise capacity [E]), score of ≥ 7
- FEV1 (i.e., forced expiratory volume in the first second) < 15% to 20% predicted
- three or more severe exacerbations during the preceding year with one severe exacerbation with acute hypercapnic respiratory failure
- moderate to severe pulmonary hypertension

**Interstitial Lung Disease (ILD):**
- a 10% or greater decrease in FVC (i.e., forced vital capacity) during six months of follow-up
- a decline in diffusion capacity (corrected for alveolar volume) ≥15% during 6 months of follow-up
- decrease in pulse oximetry <88% during a six-minute walk test
- confirmed pulmonary hypertension
- hospitalization for decline in respiratory status, pneumothorax or acute exacerbation

**Cystic Fibrosis:**
- chronic respiratory failure with hypoxia
- hypercapnia
- long-term non-invasive ventilation
- pulmonary hypertension
- frequent hospitalization
- rapid decline in lung function
- World Health Organization Functional Class IV

**Pulmonary Vascular Disease:**
- persistent NYHA functional class III or IV
- cardiac index of less than two liters per minute per square meter
- right atrial pressure of more than 15 mmHg
- low, or declining six-minute walk test (less than 350 meters)
- Development of significant hemoptysis, pericardial effusion, or signs of progressive right heart failure

**Literature Review for Lung Transplantation:** Lung transplantation recipients represent a heterogeneous population, with different diagnostic groups having different survival rates; however, in a cohort study of 1997 patients, 1143 of whom received lung transplantation, improved survival was noted for all diagnosis groups (Titman, et al., 2009). Although there are no randomized controlled clinical trials demonstrating the safety and effectiveness of lung transplantation, several registry analyses and retrospective cohort studies note improved overall survival compared with other medical and surgical therapies (Organ Procurement and Transplantation Network [OPTN], 2019; Chambers, et al., 2017; Christie, et al., 2010).

**Professional Societies/Organizations**

**American Society of Transplantation (AST) and the American Society of Transplant Surgeons (ASTS):** On behalf of the AST and ASTS, Faro et al. (2007) noted that, in general, lung transplantation should be considered in selected children with end-stage or progressive lung disease or life-threatening pulmonary vascular disease for which there is no other medical therapy.

**Heart-Lung Transplantation**

Heart-lung transplantation is the surgical replacement of the heart and lung(s) of an individual who has end-stage cardiopulmonary disease with the healthy heart and lungs of a donor. It is an accepted therapy for an individual whose disease is refractory to standard optimal medical or surgical treatment when no contraindications are present. Combined heart-lung transplantation is reserved for a candidate in whom either heart transplantation or lung transplantation alone will not improve the recipient’s condition.

**Indications for Heart-Lung Transplantation:** Indications for heart-lung transplants have changed over time. During the time period January 2004 through June 2015 the most frequent indications for heart-lung transplant were congenital heart disease, pulmonary arterial hypertension, and cardiomyopathy (Yusen, et al., 2016). Heart-lung transplantation is usually reserved for patients with uncorrectable or previously repaired or palliated congenital heart disease associated with significant pulmonary vascular obstructive disease. Such disease includes a single-ventricle physiology with pulmonary vascular disease or left ventricular (LV) dysfunction with associated pulmonary vascular disease. In the presence of more complex intracardiac abnormalities, combined heart-lung transplantation is usually most appropriate. Indications include, but are not limited to complex congenital disease with pulmonary hypoplasia, Eisenmenger syndrome, primary pulmonary hypertension, congenital lung abnormalities, alpha-antitrypsin deficiency, and end-stage parenchymal lung disease (Weill, et al., 2016; Bernstein, 2016; Warnes, et al., 2008).

**Literature Review for Heart-Lung Transplantation:** There are no randomized clinical trials comparing heart-lung transplantation to optimal medical treatment. Graft survival for primary heart-lung transplant recipients at one-, three- and five-years were 80.9%, 58.3% and 49.2%, respectively, based on Organ Procurement and Transplantation Network (OPTN) data for primary heart-lung transplants performed 2008-2015 (based on OPTN data as of July 26, 2019).

**Retransplantation**

Retransplantation remains a controversial procedure, in part due to ethical concerns over the limited supply of organs. The recipient of the retransplantation procedure often suffers from the systemic sequelae of short- or long-term immunosuppression, infection, and technical issues attributable to the initial transplantation surgery (Goldraich, et al., 2016; Kawut, et al., 2008).

Retransplantation has remained constant at 2%-4% of adult heart transplants since 1982. Cardiac allograft vasculopathy (CAV) and myopathy are the most common reasons for retransplantation (Lund, et al., 2014). Heart retransplantation is indicated for those patients who develop CAV with refractory cardiac allograft dysfunction, without evidence of ongoing rejection (Mehra, et al., 2016). Graft survival outcomes for repeat heart transplantation are 86.7%, 75.5% and 67.8% for one-, three-, and five-years, respectively, based on Organ Procurement and Transplantation network (OPTN) data as of July 26, 2019. Although outcomes are decreased for both children and adults compared to results for primary transplantation, retransplantation may be an appropriate intervention for eligible children and adults.
Outcomes after repeat lung transplantation are generally poorer than those seen with the primary transplantation procedure. Survival rates for repeat lung transplantation performed between 2008 and 2015 were 76%, 49% and 33.8%, respectively, at one-, three-, and five-years (based on OPTN data as of July 26, 2019). Although data are limited, lung retransplantation may be an appropriate therapeutic option for highly selected individuals for complications of transplantation that are refractory to other medical or surgical therapies. Survival rates were not available for repeat heart-lung transplants at one, three and five years due to the low number of transplants performed.

**Ex vivo lung perfusion (EVLP)**

Lung transplantation is a life-saving procedure for patients with end-stage lung disease. In 2016, 2692 transplant candidates age 12 years or older were added to the lung transplant waiting list and 2345 transplants were performed. The demand for lung for transplant continues be greater than the donations. A total of 9.8% of candidates 12 years of age or older died within three years of being waitlisted for transplant. Risk of waitlist mortality plays an important role in organ allocation in the US, where lungs are allocated to candidates 12 years or older based on the lung allocation score (LAS), age, geography, ABO compatibility, and, if necessary, waiting time. Candidates younger than 12 years access transplant through an illness-based priority status, age, geography, blood type (ABO) compatibility, and waiting time (Valapour, et al., 2018). A strategy to address the shortage of donor lungs is the use of marginal lungs for transplant. Ex vivo lung perfusion (ELVP) is a proposed technology to assess and prepare lungs that are considered marginal for transplantation. However there are is a lack of randomized controlled trials evaluating ELVP on marginal lungs. The rationale for normothermic ex vivo preservation as an alternative to the standard of care (cold ischemic storage) is that keeping donor lungs in a near physiologic state allows pulmonary cells and tissues to remain metabolically active and viable for additional hours between the time of cardiac death and functional evaluation by a transplant team (Hayes, 2018). EVLP is proposed to provide a window of time to evaluate and recondition lungs of inferior quality outside the donor body before transplantation. During EVLP evaluation, the lungs remain viable, as it is done at body temperature (37°C), making the lungs metabolically active and viable for hours (Makdisi, et al., 2017). Examples of lung EVLP systems are the Organ Care System™ (OCS™) Lung System, XVIVO XPS, XVIVO LS and XVIVO Disposable Lung Set.

**U.S. Food and Drug Administration (FDA):** According to the FDA, the Organ Care System (OCS™) Lung System (TransMedics, Inc., Andover, MA) received premarket approval (PMA) on March 22, 2018. Per the FDA the TransMedics® OCS Lung System “is a portable organ perfusion, ventilation, and monitoring medical device indicated for the preservation of standard criteria donor lungs in a near physiologic, ventilated, and perfused state for double lung transplantation”. The product labeling for the OCS Lung System notes that the system is contraindicated for donor lungs that have moderate to severe lung injury resulting air leak, as this could result in leakage of fluid and air at the injured area, which will compromise the ability of the OCS Lung System to maintain the donor lungs in good condition (FDA, 2018).

The XVIVO Perfusion System (XPS™) with STEEN Solution™ Perfusate (XVIVO Perfusion Inc., Englewood, CO) received premarket approval (PMA) on April 26, 2019. Per the FDA the XPS™ with STEEN Solution™ Perfusate is intended to be used on donor lungs prior to transplantation in patients with end-stage lung disease. The FDA states that “the XPS™ System warms the donor lungs to near normal body temperature and continuouslyflushes the lung tissue with the STEEN Solution™, which preserves the lungs and removes waste products.” The system is used only for previously unaccepted donor lungs that will be transplanted into a patient with end-stage lung disease (FDA, 2019).

**Literature Review:** Evidence evaluating ELVP is primarily in the form of retrospective reviews and prospective case series observational studies, review articles, and few randomized controlled trials (Hsin, et al., 2018; Makdisi, et al., 2017; Fisher, et al., 2016; Zeriouh, et al., 2016; Popov, et al., 2015).

Warnecke et al. (2018) published the results of a prospective, randomized, controlled, open-label, phase 3 trial (INSPIRE) which assessed physiological donor lung preservation using the Organ Care System (OCS) Lung device compared with cold static storage. The included patients were over 18 years old and were registered as standard criteria primary double lung transplant candidates. The eligible donors were younger than age 65, had a ratio of partial pressure of oxygen in arterial blood to the fraction of inspired oxygen of more than 300 mmHg, no active primary pulmonary disease, and were suitable for preservation with OCS or the current cold storage
standard of care. The transplant recipients were randomly assigned to receive standard criteria donor lungs preserved in the OCS Lung device (n=141) or cold storage at 4°C (n=165). The primary outcome was absence of primary graft dysfunction grade three (PGD3) within the first 72 hours after transplant and survival at day 30. The primary safety outcome was the mean number of lung graft-related serious adverse events per patient within 30 days of transplant. PGD3 was assessed at post-surgical intensive care unit admission (0 hours) and at 24, 48, and 72 hours. Long-term follow-up was measured at months six, 12, and 24. The INSPIRE study was designed to show non-inferiority of the OCS treatment to the control treatment with a 4% non-inferiority margin (OCS treatment had to perform at least five percentage points higher than the control treatment.) The primary outcome (absence of primary graft dysfunction grade three (PGD3) within the first 72 hours after transplant and survival at day 30) was met in 112/141 (79.4%) OCS patients compared to 116/165 (70.3%) control group patients (p=0.0038). The difference satisfied the predefined 4% non-inferiority test, but not a subsequent test for superiority (p=0.068). The incidence of PGD3 within 72 hours, included 25/141 (17.7%) OCS patients and 49/165 (29.7%) control group patients indicating a clinically significant lower rate of PGD3 (p=0.015) in the OCS group. Patient survival at day 30 post-transplant was 135/141 (95.7%) OCS patients and 165 (100%) control group patients, indicating a clinically significant lower rate of survival at 30 days post-transplant (p=0.009) in the OCS group. Patient survival at 12 months was 126/141 (89.4%) OCS patients compared with 146/165 (88.1%) control group patients. The primary safety endpoint was met (0.23 lung graft-related serious adverse events in the OCS group patients, indicating a clinically significant lower rate of survival at 30 days post-transplant (p=0.009) in the OCS group. Patient survival at 12 months was 126/141 (89.4%) OCS patients compared with 146/165 (88.1%) control group patients. The primary safety endpoint was met (0.23 lung graft-related serious adverse events in the OCS group compared with 0.28 events in the control group) (non-inferiority test p=0·020). Author noted limitations of the study included: its unblinded nature; randomization occurred before final acceptance of the donor lungs (n=2) ultimately did not qualify for transplant and were rejected for lung transplant owing to technical reasons. There were 76 transplants performed within this trial (ELVP, n=35; control, n=41). Donor lungs were considered standard and eligible for inclusion when they met all of the criteria. The criteria were donation after brain death, arterial oxygen partial pressure of inspired oxygen ratio (PaO2/FiO2 ratio) on100% O2 > 300 mmHg, donor age > 18 years, clear chest x-ray, no major purulent secretions found during bronchoscopy, no major mechanical lung trauma, no gross gastric aspiration, no evidence of significant infection, no evidence for human immunodeficiency virus, hepatitis virus, hepatitis C virus, or any other relevant viral disease and no history or evidence of malignant disease. All recipients on the waiting list were considered except for patients presenting with no consent, pediatric recipient < 18 years old, diagnosis of primary pulmonary arterial hypertension, patient ventilated or on mechanical support before transplant, previous transplant of any solid organ and the need for combined heart-lung transplant, lobar lung transplant or single-lung transplant. The primary study end-points were the ratio of partial pressure arterial oxygen and fraction of inspired oxygen (PaO2/FiO2 ratio) (FiO2=1.0) and primary graft dysfunction (PGD) > 1 at 24 hours after lung transplant. The secondary end-points were PaO2/FiO2 ratio and PGD scores measured at 12, 48 and 72 hours post-transplant, duration of intubation, length of ICU stay and hospitalization time. The median PaO2/FiO2 at 24 hours after transplant between the two groups was not statistically significant (p=0.63) and the difference between the two groups at all other time points did not reach statistical significance. Incidence of primary graft dysfunction > 1 was lower in the EVLP group at all times points compared with the control group and the need for post-operative prolonged extracorporeal membrane oxygenation was lower in the EVLP group, however the differences did not meet statistical significance (p=0.44, respectively). Short-term clinical outcomes did not differ between recipients in the two groups. The authors noted limitation of the study was the small patient population. The authors concluded that in a clinical setting EVLP applied in donor lungs that meet the standard acceptance criteria was at least equivalent to standard lung procurement. However, statistical significance for superiority of EVLP was not achieved in this study. The authors suggested that the focus of future studies should focus on prolonged perfusion and protocol modifications. Additional studies are needed to support the safety and effectiveness of EVLP.

Hayes (2018) published a Prognosis Overview report on the Organ Care System (OCS) Lung (TransMedics) for ex vivo lung perfusion system for the preservation of donor lungs. Hayes concluded that there is insufficient published evidence to assess the risks and benefits of the OCS Lung System over standard cold storage techniques for preservation of donor lungs. According to Hayes, there is no published evidence to date.
demonstrating that the OCS Lung improves post-transplant clinical morbidity or mortality outcomes compared with standard cold storage.

**Contraindications to Heart, Lung, and Heart-Lung Transplantation**

Many factors affect the outcome of solid organ transplantation; appropriate selection is the first step in attaining the best result for each recipient. Transplantation of the heart, lung(s) or heart and lungs remains a complex therapy; it is important, therefore, to consider the sum of all contraindications and comorbidities.

**Heart Transplantation Contraindications:** In the 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: A 10-year update, the following contraindications are noted (Mehra, et al., 2016):

- diabetes with end-organ damage
- irreversible renal dysfunction (eGFR < 30 ml/min/1.73 m2)
- symptomatic cerebrovascular disease
- elevated pulmonary vascular resistance
- severe extracardiac amyloid organ dysfunction
- chronic HCV or HBV infection, clinical, radiologic or biochemical signs of cirrhosis, portal hypertension or hepatocellular carcinoma

**Lung and Heart-Lung Transplantation Contraindications:** In the consensus document for the selection of lung transplant candidates: 2014 -an update from the Pulmonary Transplantation Council of the International Society for Heart and Lung Transplantation (Weill, et al., 2015) the following absolute contraindications are noted:

- a recent history of malignancy, (recommend a two year disease-free interval combined with a low predicted risk of recurrence after lung transplantation)
- untreated advanced dysfunction of another major organ system (e.g., heart, liver, kidney or brain)
- uncorrected atherosclerotic disease with possible end-organ ischemia or dysfunction and/or coronary artery disease not amenable to revascularization
- acute medical instability
- uncorrectable bleeding disorder
- chronic infection with highly virulent and/or resistant microbes
- active Mycobacterium tuberculosis infection
- chest wall or spinal deformity expected to cause severe restriction after transplantation
- class II or III obesity
- current non-adherence to medical therapy or a history of non-adherence
- psychiatric or psychologic conditions associated with the inability to cooperate with care
- absence of a consistent and reliable social support system
- severely limited functional status with poor rehabilitation potential
- substance abuse or dependence

In addition to absolute contraindications, there are relative contraindications as well which include (list is not all inclusive):

- age
- obesity
- malnutrition
- severe osteoporosis
- extensive prior chest surgery with lung resection
- active infections
- other medical conditions should be treated before transplantation (diabetes, hypertension)

**Centers for Medicare & Medicaid Services (CMS)**
National Coverage Determinations (NCDs): National Coverage Determination (NCD) for Heart Transplants (260.9). Effective date 5/1/2008. It is broader in scope than the Coverage Policy. Refer to the CMS NCD table of contents link in the reference section.

Local Coverage Determinations (LCDs): No Local Coverage Determinations found.

Use Outside of the US:
The Canadian Cardiovascular Society Consensus conference update on cardiac transplantation (Haddad, et al., 2009) indicated that cardiac transplantation is the treatment of choice for patients who have severe end-stage heart failure and/or complex congenital heart disease despite maximal medical or surgical therapy and who have an unacceptable quality of life and poor anticipated survival. Patients with extracardiac disease are not eligible for a heart transplant if the procedure would significantly reduce their expected lifespan. Furthermore, a patient would not be a candidate for transplantation if the condition is expected to be exacerbated by the post-transplant use of immunosuppressive agents or there is no significant rehabilitation potential.

The Heart Failure Association (HFA) of the European Society of Cardiology (ESC) issued a position statement on advanced heart failure (Crespo-Leiro, et al., 2018) which indicated that heart transplantation remains the treatment of choice for patients with advanced or end-stage heart failure without contraindications. Data from the latest International Society for Heart and Lung Transplantation (ISHLT) Registry showed one-year survival of around 90% and median survival of 12.2 years. Transplantation not only improves survival but also functional status and quality of life (Lund, et al., 2014). Contraindications included active infection, severe peripheral arterial/cerebrovascular disease, pharmacologic irreversible pulmonary hypertension, cancer, irreversible renal dysfunction, systemic disease with multi-organ involvement, other serious co-morbidity with poor prognosis, pre-transplant BMI > 35 kg/m², current alcohol or drug abuse and any patient for whom social supports are deemed insufficient.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

<table>
<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>32850</td>
<td>Donor pneumonectomy(s) (including cold preservation), from cadaver donor</td>
</tr>
<tr>
<td>32851</td>
<td>Lung transplant, single; without cardiopulmonary bypass</td>
</tr>
<tr>
<td>32852</td>
<td>Lung transplant, single; with cardiopulmonary bypass</td>
</tr>
<tr>
<td>32853</td>
<td>Lung transplant, double (bilateral sequential or en bloc); without cardiopulmonary bypass</td>
</tr>
<tr>
<td>32854</td>
<td>Lung transplant, double (bilateral sequential or en bloc); with cardiopulmonary bypass</td>
</tr>
<tr>
<td>32855</td>
<td>Backbench standard preparation of cadaver donor lung allograft prior to transplantation, including dissection of allograft from surrounding soft tissues to prepare pulmonary venous/atrial cuff, pulmonary artery, and bronchus; unilateral</td>
</tr>
<tr>
<td>32856</td>
<td>Backbench standard preparation of cadaver donor lung allograft prior to transplantation, including dissection of allograft from surrounding soft tissues to prepare pulmonary venous/atrial cuff, pulmonary artery, and bronchus; bilateral</td>
</tr>
<tr>
<td>33929</td>
<td>Removal of a total replacement heart system (artificial heart) for heart transplantation (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>33930</td>
<td>Donor cardiectomy-pneumonectomy (including cold preservation)</td>
</tr>
<tr>
<td>33933</td>
<td>Backbench standard preparation of cadaver donor heart/lung allograft prior to transplantation, including dissection of allograft from surrounding soft tissues to prepare aorta, superior vena cava, inferior vena cava, and trachea for implantation</td>
</tr>
<tr>
<td>33935</td>
<td>Heart-lung transplant with recipient cardiectomy-pneumonectomy</td>
</tr>
<tr>
<td>33940</td>
<td>Donor cardiectomy (including cold preservation)</td>
</tr>
<tr>
<td>33944</td>
<td>Backbench standard preparation of cadaver donor heart allograft prior to transplantation, including dissection of allograft from surrounding soft tissues to prepare aorta, superior vena cava, inferior vena cava, pulmonary artery, and left atrium for implantation</td>
</tr>
<tr>
<td>33945</td>
<td>Heart transplant, with or without recipient cardiectomy</td>
</tr>
</tbody>
</table>

### HCPCS Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>S2152</td>
<td>Solid organ(s), complete or segmental, single organ or combination of organs; deceased or living donor(s), procurement, transplantation, and related complications; including: drugs; supplies; hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services, and the number of days of pre- and post-transplant care in the global definition</td>
</tr>
<tr>
<td>S2060</td>
<td>Lobar lung transplantation</td>
</tr>
<tr>
<td>S2061</td>
<td>Donor lobectomy (lung) for transplantation, living donor</td>
</tr>
</tbody>
</table>

Considered Experimental, Investigational or Unproven when used to report Ex-vivo lung perfusion (e.g., Organ Care System™) for lung transplantation:

### CPT® Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0494T</td>
<td>Surgical preparation and cannulation of marginal (extended) cadaver donor lung(s) to ex vivo organ perfusion system, including decannulation, separation from the perfusion system, and cold preservation of the allograft prior to implantation, when performed</td>
</tr>
<tr>
<td>0495T</td>
<td>Initiation and monitoring marginal (extended) cadaver donor lung(s) organ perfusion system by physician or qualified health care professional, including physiological and laboratory assessment (eg, pulmonary artery flow, pulmonary artery pressure, left atrial pressure, pulmonary vascular resistance, mean/peak and plateau airway pressure, dynamic compliance and perfusate gas analysis), including bronchoscopy and X ray when performed; first two hours in sterile field</td>
</tr>
<tr>
<td>0496T</td>
<td>Initiation and monitoring marginal (extended) cadaver donor lung(s) organ perfusion system by physician or qualified health care professional, including physiological and laboratory assessment (eg, pulmonary artery flow, pulmonary artery pressure, left atrial pressure, pulmonary vascular resistance, mean/peak and plateau airway pressure, dynamic compliance and perfusate gas analysis), including bronchoscopy and X ray when performed; each additional hour (List separately in addition to code for primary procedure)</td>
</tr>
</tbody>
</table>


### References


