Lung Transplantation
Clinical Coverage Criteria

Description

Lung transplantation involves the surgical replacement of one or both lungs in patients with end-stage lung diseases. Lung transplantation is typically preceded by medical interventions such as surgery or oxygen therapy. The type of lung transplantation (lobar, single, double) is based upon the candidate's condition and indication for transplantation in addition to the availability of viable donor organs. Donor organs are often scarce or unsuitable for transplantation.

Policy

This Policy applies to the following Fallon Health products:

☒ Fallon Medicare Plus, Fallon Medicare Plus Central (Medicare Advantage)
☒ MassHealth ACO
☒ NaviCare HMO SNP (Dual Eligible Medicare Advantage and MassHealth)
☒ NaviCare SCO (MassHealth-only)
☒ PACE (Summit Eldercare PACE, Fallon Health Weinberg PACE)
☒ Community Care (Commercial/Exchange)

Lung Transplantation requires prior authorization.

Medicare Advantage
Fallon Health complies with CMS's national coverage determinations (NCDs), local coverage determinations (LCDs) of Medicare Contractors with jurisdiction for claims in the Plan's service area, and applicable Medicare statutes and regulations when making medical necessity determinations for Medicare Advantage members. When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, Fallon Health may create internal coverage criteria under specific circumstances described at § 422.101(b)(6)(i) and (ii).

Medicare statutes and regulations do not have criteria for lung transplantation. Medicare does not have an NCD for lung transplantation. National Government Services, Inc., the Part A/B Medicare Administrative Contractor (MAC) with jurisdiction in our service area, does not have an LCD for lung transplantation (MCD search 03/24/2024).

To date, the Medicare program has not issued an NCD on lung or heart-lung transplantation. However, CMS established a national coverage policy for lung transplants in Federal Register / Vol. 60, No. 22 / Thursday, February 2, 1995 / Notices, Medicare Program; Criteria for Medicare Coverage of Lung Transplants.

Medicare will cover lung transplants only for those beneficiaries who are diagnosed as having progressive end-stage pulmonary disease and when performed by a facility that has received approval from CMS for a lung transplant program. Medicare will also cover lung transplantation for end-stage cardiopulmonary disease when it is expected that transplant of the lung will result in improved cardiac function.

Careful patient selection for lung transplants is essential to achieve optimal results. CMS requires that facilities have written patient selection criteria that they follow in determining suitable candidates for lung transplants, such as the following:

a. A patient is selected based upon both a critical medical need for transplantation and a strong likelihood of successful clinical outcome.
b. A patient who is selected for a lung transplant has irreversible, progressively disabling, end-stage pulmonary disease (or, in some instances, end-stage cardiopulmonary disease).
c. The facility has tried or considered all other medically appropriate medical and surgical therapies that might be expected to yield both short- and long-term survival comparable to that of transplantation.
d. Plans for long-term adherence to a disciplined medical regimen are feasible and realistic for the individual patient.

Many factors must be recognized as exerting an adverse influence upon the patient's outcome after transplantation. The following adverse factors are among those that should be considered in selecting patients for transplantation:

- Primary or metastatic malignancies of the lung.
- Current significant acute illness that is likely to contribute to a poor outcome if the patient receives a lung transplant or current use of mechanical ventilation for more than a very brief period.
- Significant or advanced heart, liver, kidney, gastrointestinal or other systemic or multi-system disease that is likely to contribute to a poor outcome after lung transplantation.
- Significant extra-pulmonary infection.
- Chronic pulmonary infection in candidates for single lung transplantation.
- Continued cigarette smoking or failure to have abstained for long enough to indicate low likelihood of recidivism.
- Systemic hypertension that requires more than two drugs for adequate control.
- Cachexia, even in the absence of major end-organ failure.
- Obesity.
- Previous thoracic or cardiac surgery or other bases for pleural adhesions.
- Age beyond that at which there has been substantial favorable experience.
- Chronic corticoid therapy that cannot be tapered to a low dose (10 mg prednisone per day) or discontinued prior to transplantation.
- A history of behavior pattern or psychiatric illness considered likely to interfere significantly with a disciplined medical regimen.

The transplant must be performed by a facility that has received approval from CMS for an organ transplant program. The List of CMS-Approved Organ Transplant Programs is currently available on the Quality, Certification and Oversight Reports (QCOR) web site. The list may be downloaded in Microsoft Excel format. Click "Resources" at the top of the main QCOR page. Select "List of CMS-Approved Organ Transplant Programs" link.

MassHealth

Fallon Health follows Medical Necessity Guidelines published by MassHealth when making medical necessity determinations for MassHealth members. In the absence of Medical Necessity Guidelines published by MassHealth, Fallon Health may create clinical coverage criteria in accordance with the definition of Medical Necessity in 130 CMR 450.204.

MassHealth has Guidelines for Medical Necessity Determination for Organ Transplant Procedures. These Guidelines apply to the following single- or double-organ transplants: liver, heart, lung, pancreas, and small bowel (MassHealth website search 03/24/2024), therefore, Fallon Health Clinical Coverage Criteria for lung transplantation are not applicable.

NaviCare HMO SNP, NaviCare SCO
For plan members enrolled in NaviCare, Fallon Health first follow's CMS's national coverage determinations (NCDs), local coverage determinations (LCDs) of Medicare Contractors with jurisdiction for claims in the Plan's service area, and applicable Medicare statutes and regulations when making medical necessity determinations.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, or if the NaviCare member does not meet coverage criteria in applicable Medicare statutes, regulations, NCDs or LCDs, Fallon Health then follows Medical Necessity Guidelines published by MassHealth when making necessity determinations for NaviCare members.

PACE (Summit Eldercare PACE, Fallon Health Weinberg PACE)
Each PACE plan member is assigned to an Interdisciplinary Team. PACE provides participants with all the care and services covered by Medicare and Medicaid, as authorized by the interdisciplinary team, as well as additional medically necessary care and services not covered by Medicare and Medicaid. With the exception of emergency care and out-of-area urgently needed care, all care and services provided to PACE plan members must be authorized by the interdisciplinary team.

Fallon Health Clinical Coverage Criteria

Lung transplantation is considered medically necessary for adults with chronic, end-stage lung disease who meet all of the following general criteria:

1. High (>50%) risk of death from lung disease within 2 years if lung transplantation is not performed;
2. High (>80%) likelihood of 5-year post-transplant survival from a general medical perspective provided that there is adequate graft function; and
3. Does not have any of the following Absolute Contraindications[1]:
    - Lack of patient willingness or acceptance of transplant
    - Malignancy with high risk of recurrence or death related to cancer
    - Glomerular filtration rate <40 mL/min/1.73m2 unless being considered for multi-organ transplant
    - Acute coronary syndrome or myocardial infarction within 30 days (excluding demand ischemia)
    - Stroke within 30 days
    - Liver cirrhosis with portal hypertension or synthetic dysfunction unless being considered for multi-organ transplant
    - Acute liver failure
    - Acute renal failure with rising creatinine or on dialysis and low likelihood of recovery
    - Septic shock
    - Active extrapulmonary or disseminated infection
    - Active tuberculosis infection
    - HIV infection with detectable viral load
    - Limited functional status (e.g. non-ambulatory) with poor potential for post-transplant rehabilitation
    - Progressive cognitive impairment

[1] Lung transplant candidates with one of these Absolute Contraindications are considered too high risk to achieve successful outcomes post lung transplantation. These conditions significantly increase the risk of an adverse outcome post-transplant and/or would make transplant most likely harmful for a recipient (Leard et al., 2021). Risk factors can change over time and may not be a contraindication for referral, but when present at the time of listing or while listed for lung transplantation may increase risk for poor transplant outcomes.

- Repeated episodes of non-adherence without evidence of improvement (For pediatric patients this is not an absolute contraindication and ongoing assessment of non-adherence should occur as they progress through different developmental stages.)
- Active substance use or dependence including current tobacco use, vaping, marijuana smoking, or IV drug use
    - The member must be a non-smoker and drug free for the previous 6 months or greater. The member should receive counseling for any previous substance use issues in order to maintain abstinence. Convincing evidence of risk reduction behaviors, such as meaningful and/or long-term participation in therapy for substance abuse and/or dependence, may be required before offering lung transplantation. Serial blood and urine testing can be used to verify abstinence from substances that are of concern.
- Other severe uncontrolled medical condition expected to limit survival after transplant

Chronic, end-stage lung disease includes, but is not limited to, the following diagnoses:
- Alpha-1 antitrypsin deficiency
- Bronchiectasis
- Bronchopulmonary dysplasia
- Chronic obstructive pulmonary disease/emphysema
- Cystic fibrosis
- Eisenmenger's syndrome
- Eosinophilic granuloma
- Idiopathic pulmonary fibrosis
- Lymphangiomyomatosis
- Pulmonary hypertension/pulmonary arterial Hypertension
- Sarcoidosis
- Scleroderma

It is important to note that referral and listing for lung transplant are two different entities. The International Society for Heart and Lung Transplantation (ISHLT) recommends early referral to a transplant center for progressive lung diseases that have a projected poor prognosis. Early referral may allow time for candidates to address modifiable barriers to transplant, such as obesity, malnutrition, medical comorbidities, or inadequate social support. Referral means that a patient has met the minimal clinical criteria and further consideration towards lung transplant should be considered in the absence of any absolute contraindications. Listing, on the other hand, requires a thorough evaluation and careful risk-to-benefit assessment. In general, listing a patient for lung transplant is thought to be an explicit acknowledgment that a patient has limited life expectancy without lung transplant and the odds of survival are better with lung transplant (Shweish and Dronavalli, 2019).

2021 Consensus ISHLT Timing of Listing for Some Chronic, End-Stage Lung Diseases
(Leard et al., 2021)
Chronic Obstructive Pulmonary Disease (COPD), adults ≥ 18 years of age:
- BODE score 7-10
- Additional factors that may prompt listing include:
    - FEV1 < 20% predicted
    - Presence of moderate to severe pulmonary hypertension
    - History of severe exacerbations
    - Chronic hypercapnia

Interstitial Lung Disease, adult ≥ 18 years of age:
- Any form of pulmonary fibrosis with one of the following in the past 6 months despite appropriate treatment:
    - Absolute decline in FVC > 10%
    - Absolute decline in DLCO > 10%

    - Absolute decline in FVC > 5% with radiographic progression.
- Desaturation to < 88% on 6 minute walk test or > 50 m decline in 6 minute walk test distance in the past 6 months
- Pulmonary hypertension on right heart catheterization or 2-dimensional echocardiography (in the absence of diastolic dysfunction)
- Hospitalization because of respiratory decline, pneumothorax, or acute exacerbation.

Cystic Fibrosis (CF), adults ≥ 18 years of age:
Referral for lung transplantation should occur for an individual with CF meeting any of the following criteria despite optimal medical management including a trial of elexacaftor, tezacaftor, and ivacaftor if eligible:
- FEV1 < 30% predicted in adults[2]
- FEV1 < 40% predicted in adults and any of the following:
    - Six-minute walk distance < 400 meters
    - PaCO2 > 50 mmHg
    - Hypoxemia at rest or with exertion
    - Pulmonary hypertension (PA systolic pressure > 50 mmHg on echocardiogram or evidence of right ventricular dysfunction)
    - Worsening nutritional status despite supplementation
    - 2 exacerbations per year requiring intravenous antibiotics
    - Massive hemoptysis (>240 mL) requiring bronchial artery embolization
    - Pneumothorax
- FEV1 < 50% predicted and rapidly declining based on pulmonary function testing or progressive symptoms
- Any exacerbation requiring positive pressure ventilation

Listing for lung transplantation should occur for an individual with CF meeting any of the above referral criteria in combination with any of the following:
- FEV1 < 25% predicted
- Rapid decline in lung function or progressive symptoms (>30% relative decline in FEV1 over 12 months)
- Frequent hospitalization, particularly if > 28 days hospitalized in the preceding year
- Any exacerbation requiring mechanical ventilation
- Chronic respiratory failure with hypoxemia or hypercapnia, particularly for those with increasing oxygen requirements or needing long-term non-invasive ventilation therapy
- Pulmonary hypertension (Pulmonary arterial systolic pressure > 50 mmHg on echocardiogram or evidence of right ventricular dysfunction)
- Worsening nutritional status particularly with BMI < 18 kg/m^2 despite nutritional interventions
- Recurrent massive hemoptysis despite bronchial artery embolization
- World Health Organization functional class IV

Non-CF Bronchiectasis, adults ≥ 18 years of age:
For individuals with non-CF bronchiectasis, similar criteria as with CF for referral and listing for lung transplantation is reasonable, though providers should recognize that prognosis is highly variable with many patients experiencing a more stable course.

Pulmonary Arterial Hypertension (PAH), adults ≥ 18 years of age:
- ESC/ERS high risk or REVEAL risk score >10 on appropriate PAH therapy, including IV or SC prostacyclin analogues

[2] There have been many studies that have developed predictive models for CF mortality; however, forced expiratory volume in 1 second (FEV_1) <30% predicted remains the most commonly used indicator of 2-year survival, and CF clinicians generally use the 30% FEV_1 threshold to guide patient referrals for lung transplantation assessment (Stanojevic et al., 2019).

- Progressive hypoxemia, especially in patients with PVOD or PCH
- Progressive, but not end-stage, liver or kidney dysfunction due to PAH
- Life-threatening hemoptysis

Lymphangioleiomyomatosis (LAM), adults ≥ 18 years of age:
Referral for lung transplantation evaluation should occur for an individual with LAM who has any of the following despite mTOR inhibitor therapy:
- Severely abnormal lung function (e.g. FEV_1 < 30% predicted)
- Exertional dyspnea (NYHA class III or IV)
- Hypoxemia at rest
- Pulmonary hypertension
- Refractory pneumothorax

Timing of Listing
Listing for lung transplantation should occur for an individual with LAM who meets the above referral criteria and has evidence of disease progression despite mTOR inhibitor therapy.

Cessation of mTOR inhibitor therapy should occur at the time of transplant but cessation should not be required for placement on the waiting list. It may be preferable to use everolimus and target trough levels in the lower therapeutic range for patients on the waiting list.

Thoracic Malignancy, adults ≥ 18 years of age:
(1) Lung transplant should be limited to very select cases of lung-limited adenocarcinoma in situ, minimally invasive adenocarcinoma, or lepidic predominant adenocarcinoma for patients in whom (1) surgical resection is not feasible either because of multifocal disease or significant underlying pulmonary disease;
(2) multifocal disease has resulted in significant lung restriction and respiratory compromise;
(3) medical oncology therapies have failed or are contraindicated; and
(4) lung transplant is expected to be curative.

Acute Respiratory Distress Syndrome (ARDS), adults ≥ 18 years of age:
Persistent requirement for mechanical ventilatory support and /or ECLS without expectation of clinical recovery and with evidence of irreversible lung destruction.

Indications for Lung Transplant in Children
The etiology of lung disease among pediatric candidates has changed over time, with a decrease in the proportion of candidates with cystic fibrosis from 40.0% in 2017 to 9.7% in 2022. Cystic Fibrosis remains the leading indication for lung transplant in children aged 6–17 years; however, the number of candidates with idiopathic pulmonary arterial hypertension (IPAH) is increasing, and it is currently the most common indication for those 1–5 years of age. For infants (< 1 year) surfactant protein B deficiency and pulmonary hypertension (which is usually due to congenital heart disease, not IPAH) are the primary indications for lung transplant. Other infant and childhood indications include adenosine triphosphate binding cassette protein member A3 deficiency, alveolar capillary dysplasia with misalignment of pulmonary veins, childhood interstitial lung disease, and bronchiolitis obliterans (Leard et al., 2021).

Timing of Listing
In addition to the general criteria for adults, considerations for listing children for lung transplant include the following:
- Children with Cystic Fibrosis (CF) < 18 years of age should be listed when FEV_1 < 30% predicted.

- Patients with pulmonary arterial hypertension (PAH) <18 years of age should be listed when they are in the European Pediatric Pulmonary Vascular Disease Network (EPPVDN) high risk category[3] and on optimal therapy without improvement.

Risk Factors to be Considered
Because lung transplantation is a complex therapy with a significant risk of perioperative morbidity and mortality, it is important to risk factors for poor transplant outcomes in addition to the Absolute Contraindications listed above. It is essential to account for medical comorbidities, psychosocial factors, and potential for rehabilitation in the evaluation of transplant candidates. While it is important to consider the relative risk associated with a particular risk factor (e.g., increasing age or obesity), it is also relevant to think about the cumulative effect of multiple potential risk factors (Leard et al., 2021).

Risk Factors With High or Substantially Increased Risk - Candidates with these conditions may be considered in centers with expertise specific to the condition. Data to support transplanting patients with these risk factors may not be available or there is substantially increased risk based upon the currently available data, and further research is needed to better inform future recommendations. When more than one of these risk factors are present, they are thought to be possibly multiplicative in terms of increasing risk of adverse outcomes. Modifiable conditions should be optimized when possible.

Risk factors - Risk factors with implications for short and/or long term outcomes after transplant with implications for short and/or long term outcomes after transplant. While it is acceptable for lung transplant programs to consider patients with these risk factors, multiple risk factors together may increase risk for adverse post lung transplant outcomes.

Risk Factors With High or Substantially Increased Risk	Risk factors
Age over 70 years*	Age 65–70 years*
Severe coronary artery disease that requires coronary artery bypass grafting at transplant	Glomerular filtration rate 40–60 mL/min/1.73m^2
Reduced left ventricular ejection fraction <40%	Mild to moderate coronary artery disease
Significant cerebrovascular disease	Severe coronary artery disease that can be revascularized via percutaneous coronary intervention prior to transplant
Severe esophageal dysmotility	Patients with prior coronary artery bypass grafting
Untreatable hematologic disorders including bleeding diathesis, thrombophilia, or severe bone marrow dysfunction	Reduced left ventricular ejection fraction 40–50%
BMI greater than or equal to 35 kg/m^2	Peripheral vascular disease
BMI <16 kg/m2	Connective tissue diseases (scleroderma, lupus, inflammatory myopathies)
Limited functional status with potential for post-transplant rehabilitation	Severe gastroesophageal reflux disease
Psychiatric, psychological or cognitive conditions with potential to interfere with medical adherence without sufficient support systems	Esophageal dysmotility
Unreliable support system or caregiving plan	Thrombocytopenia, leukopenia, or anemia with high likelihood of persistence after transplant

[3] Hansmann G, Koestenberger M, Alastalo TP, et al. 2019 updated consensus statement on the diagnosis and treatment of pediatric pulmonary hypertension: The European Pediatric Pulmonary Vascular Disease Network (EPPVDN), endorsed by AEPC, ESPR and ISHLT. *J Heart Lung Transplant*. 2019 Sep;38(9):879-901.

Lack of understanding of disease and/or transplant despite teaching	Osteoporosis
Mycobacterium abscessus infection	BMI 30–34.9 kg/m^2
Lomentospora prolificans infection	BMI 16–17 kg/m^2
Burkholderia cenocepacia or gladioli infection	Frailty
Hepatitis B or C infection with detectable viral load and liver fibrosis	Hypoalbuminemia
Chest wall or spinal deformity expected to cause restriction after transplant	Diabetes on insulin that is poorly controlled
Extracorporeal life support	Edible marijuana use
Retransplant <1 year following initial lung transplant	*Scedosporium apiospermum* infection
Retransplant for restrictive chronic lung allograft dysfunction (CLAD)	HIV infection with undetectable viral load
Retransplant for AMR as etiology for CLAD	Previous thoracic surgery
	Prior pleurodesis
	Mechanical ventilation
	Retransplant >1 year for obstructive CLAD

* Consideration of an upper age limit for lung transplant candidacy remains a controversial subject. The age of lung transplant recipients has increased over the past decade. In the United States, candidates greater than 65 years of age now comprise more than 30% of the waiting list and are the age group with the highest transplant rate. With increasing experience in older recipients, several studies have shown that carefully selected older recipients may have the same short-term survival as younger recipients. However, the results are skewed by selection bias, reflecting the fact that most recipients over the age of 65 years undergoing lung transplant are highly selected with very few comorbidities such as coronary artery disease and diabetes. Despite this selection bias and acceptable short-term outcomes, lung transplant recipients over the age of 70 years have decreased longer term survival (Leard et al., 2021).

In regard to bilateral lung transplantation, further consideration will be given to the member's type of end-stage lung disease, specifically if it requires a bilateral rather than a single transplant.

Additionally the member's ability to tolerate the procedure and other conditions, such as cardiac dysfunction, will be considered in any review.

Lobar lung transplantation
Potential candidates with small chest size may be candidates for lobar lung transplant. While early complications may be higher, the 1- and 3- year survival may be comparable to conventional transplant, suggesting lobar lung transplant may be an acceptable option (Leard et al., 2021).

Multi-Organ Transplantation
For multi-organ transplant requests, criteria must be met for each organ requested.

- Heart-lung and other multi-organ transplantation should be limited to centers with experience in such procedures and where specialists are available to manage each of the transplanted organs.
- 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.
- Waiting times are likely to be longer and the likelihood of receiving a transplant is reduced when an individual requires more than one organ. Thus, referral should occur earlier in the disease course if multi-organ transplantation may be considered.

Lung Re-Transplantation
Lung re-transplantation will be considered on an individual case-by-case basis. The outcomes after re-transplants are inferior compared to first lung transplants, particularly if the re-transplant is done within the first year after the original transplant or for patients with restrictive allograft syndrome. Studies, however, have found acceptable results for carefully selected recipients. In the pre-transplant evaluation of such patients, particular emphasis should be focused on understanding the possible reasons for the graft failure, such as alloimmunization, poor compliance, GER, or repeated infections (Leard et al., 2021).

- The timing of re-transplant is a complex issue and requires consideration of the rate of deterioration, time since initial transplant, the need for supportive therapies and donor lung availability, which may be limiting in some cases.
- Survival after re-transplant is inferior to that seen with the primary operation and should only be undertaken in carefully selected candidates.
- In the evaluation of patients being considered for lung re-transplant, particular emphasis should be focused on understanding the possible reasons for the graft failure, such as alloimmunization, poor adherence, gastroesophageal reflux, or repeated infections.

Due to the lack of suitable donor lungs for those on the waiting list new methods are being attempted in order to increase the amount of usable donor lungs. One such method is Ex Vivo Lung Perfusion (EVLP) which attempts to maintain the lung through perfusion and ventilation after it is removed from the donor until suitable for transplantation. However this technology is new and still in the clinical trial stage. Fallon Health's Clinical Trial Payment Policy details rules surrounding coverage for member's who enroll in a qualified clinical trial: **Clinical Trials Payment Policy**.

Exclusions

- Lung transplants that do not meet the above criteria.
- Lung transplant where the member has an absolute contraindication.

Evidence Summary

Lung transplantation is now a generally accepted treatment for the management of a wide range of severe lung disorders, with evidence supporting quality of life and survival benefit for lung transplant recipients. However, the number of donor organs available remains far fewer than the number of patients with end-stage lung disease who might potentially benefit from the procedure. It is of primary importance, therefore, to optimize the use of this resource, such that the selection of patients who receive a transplant represents those with realistic prospects of favorable long-term outcomes. There is a clear ethical responsibility to respect these altruistic gifts from all donor families and to balance the medical resource requirements of one potential recipient against those of others in their society (Orens et al., 2006).

It is important to recognize that few data exist from randomized controlled trials upon which to support coverage criteria for lung transplantation. Guidelines are based primarily on consensus of opinion rendered by experts in the field and on analysis of retrospective single-center and multicenter studies and registries. The definitive work addressing criteria for selecting lung transplant patients, and contraindications against performing surgery, are written by the Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation (ISHLT), which published versions in 1998 (Maurer et al., 1998), 2006 (Orens et al., 2006), and 2014 (Weill et al., 2015). In 2021, the ISHLT updated its consensus document on selection of lung transplant candidates (Leard, 2021). While lung transplantation aims to improve both survival and quality of life, the expert consensus acknowledges that when making recommendations about allocating a scare resource, survival benefit is prioritized based on an ethical framework. The worldwide scarcity of donor lungs requires rationing of this lifesaving but limited societal resource. This makes the selection of transplant candidates an ethical choice as well as a medical one. The fundamental ethical principles of "utility", "justice", and "respect for

persons" must, therefore, provide the framework for candidate selection and organ allocation systems (Leard et al., 2021).

Over the last 3 decades, there has been a significant increase in the number of lung transplants performed, with the main trend seen in adult bilateral lung transplant. A recent report by the registry of ISHLT listed all lung transplants performed between 1995 and 2015. The most common indications consisted of COPD (36.5%), interstitial lung disease (ILD) (29.7%), and bronchiectasis (18.5%) (Yusen et al., 2016). Of these three broad categories, COPD without alpha-1 antitrypsin deficiency, idiopathic interstitial pneumonia (IIP), and CF comprised the bulk of lung transplant, respectively (Shweish and Dronavalli, 2019).

Given the high risk and complexity of lung transplant, careful assessment of potential contraindications should be made. The most recent ISHLT consensus cites several absolute contraindications for lung transplant (Leard, 2021). Candidates with these conditions are considered too high risk to achieve successful outcomes post lung transplantation. Contraindications can change over time and may not be a contraindication for referral, but when present at the time of listing or while listed for lung transplantation may increase risk for poor transplant outcomes. In addition to Absolute Contraindications, the ISHLT consensus includes risk factors with high or substantially increased risk and risk factors. Modifiable conditions should be optimized when possible.

Consideration of an upper age limit for lung transplant candidacy remains a controversial subject. In the 2006 and 2014 ISHLT guidelines, age greater than 65 years in association with low physiologic reserve and/or other relative contraindications was considered a relative contraindication. There has been no endorsement of an upper age limit as an absolute contraindication, but older individuals have worse long-term survival following lung transplant. The age of lung transplant recipients has increased over the past decade. In the United States, candidates greater than 65 years of age now comprise more than 30% of the waiting list and are the age group with the highest transplant rate. With increasing experience in older recipients, several studies have shown that carefully selected older recipients may have the same short-term survival as younger recipients. However, the results are skewed by selection bias, reflecting the fact that most recipients over the age of 65 years undergoing lung transplant are highly selected with very few comorbidities such as coronary artery disease and diabetes. Despite this selection bias and acceptable short-term outcomes, lung transplant recipients over the age of 70 years have decreased longer term survival (Hayanga et al., 2015).

Lung diseases are characterized by the Organ Procurement and Transplantation Network (OPTN) into four main diagnosis groups: group A, obstructive lung disease; group B, pulmonary vascular disease; group C, cystic fibrosis and immunodeficiency disorders; and group D, restrictive lung diseases (OPTN, 2023).

Group A, obstructive lung disease includes COPD, Alpha-1 antitrypsin deficiency, Lymphangioleiomyomatosis (LAM), Sarcoidosis with mean pulmonary artery pressure ≤30 mmHg, and bronchiectasis including primary ciliary dyskinesia.

COPD is the most common indication for lung transplant worldwide, accounting for more than one third of all lung transplants between 1995 and 2013 (Yusen et al., 2016). Several factors play into the decision to refer COPD patients for lung transplant, the most important of which are indicators of worsening functional status and spirometry. Compared to other chronic lung diseases, COPD poses a unique challenge for lung transplant. The goal in every candidate is to identify a time in the course of the disease when the patient is most likely to have a net survival benefit from lung transplant. This proves to be more challenging in COPD for several reasons. First, due to the chronicity and protracted course of COPD, patients may tend to live beyond the median post-transplant survival. Second, the lung allocation score (LAS) is designed to identify and prioritize patients with shorter survival. This means that COPD patients listed for lung transplant will end up having lower LAS and longer waitlist times. This, in turn, will lead to disease progression, physical

deconditioning and ultimately, higher risk for worse post-transplant outcomes (Shweish and Dronavalli, 2019).

Group B, pulmonary vascular disease, includes idiopathic or primary pulmonary arterial hypertension, Eisenmenger's syndrome, chronic thromboembolic disease related pulmonary hypertension, and pulmonary veno-occlusive disease.

The number of lung transplants for pulmonary arterial hypertension (PAH) has seen a decrease over the last two decades, and this is largely due to the improved survival with medical therapy for PAH. Lung transplant is indicated for patients who show evidence of persistent deterioration despite aggressive and optimized medical treatment. Despite improvements in targeted medical therapy, PAH still has a relatively poor prognosis. The timing for referral in PAH patients remains a challenge, and the window of transplant can be narrow. In addition, patients with pulmonary hypertension have higher rates of perioperative complications, manifested by higher rates of primary graft dysfunction and right ventricular failure (Shweish and Dronavalli, 2019). The Registry to Evaluate Early and Long-term PAH Disease Management (REVEAL) report identified and confirmed several risk factors associated with higher mortality (Benza et al., 2010).

Group C, infectious lung disease, includes Cystic Fibrosis (CF) and immune deficiency syndromes like IgG deficiency.

Despite the significantly improved survival in CF over the last decades, many patients continue to have progressive disease and require lung transplant. Compared to other indications for lung transplant, the 5-year lung transplant survival rates in CF are significantly better. This is largely due to the younger age of CF patients at the time of transplant. In addition, studies report improved quality of life among transplant recipients for CF. In patients who meet criteria for referral, a careful assessment should be made to determine their predicted survival and timing of transplant, which is not clearly demarcated. Several factors have been associated with increased mortality in CF patients, the most useful of which has been the FEV_1 as a surrogate for disease progression and mortality (Shweish and Dronavalli, 2019). There have been many studies that have developed predictive models for CF mortality; however, forced expiratory volume in 1 second (FEV_1) <30% predicted remains the most commonly used indicator of 2-year survival, and CF clinicians generally use the 30% FEV_1 threshold to guide patient referrals for lung transplantation assessment (Stanojevic et al., 2019).

Group D, restrictive lung disease, includes Idiopathic pulmonary fibrosis (IPF), Eosinophilic granulomatosis, Sarcoidosis with mean pulmonary artery pressure ≥30 mmHg, Scleroderma/CREST syndrome, Bronchoalveolar carcinoma, Bronchiolitis obliterans syndrome (BOS) following lung transplant, and primary graft failure following lung transplant.

IPF is a rapidly progressive disease with a median survival of 2–3 years from the time of diagnosis and a 5-year survival of about 25%. IPF is the most common subtype of interstitial lung disease (ILD) and has been associated with worse outcomes when compared to other forms of ILD. Other ILD that may carry a similar course as IPF include fibrotic non-specific interstitial pneumonia (NSIP), progressive ILDs refractory to immunomodulation therapy. The high mortality in IPF, along with the implementation of the LAS has been responsible for the dramatic increase in the number of lung transplant recipients with IPF over the last two decades and warrants earlier referral for lung transplant evaluation. Despite FDA approval of the anti-fibrotic agents nintedanib and pirfenidone, no medical therapy has been shown to have a clearly established impact on mortality. Mortality predictors in IPF have been well studied, however, these variables do not reliably predict the risk of disease progression. As of now, there are no biomarkers that have been conclusively shown to have a correlation with disease progression or mortality (Shweish and Dronavalli, 2019).

Analysis of Evidence (Rationale for Determination)

Few data exist from randomized controlled trials upon which to support coverage criteria for lung transplantation. Despite that, lung transplantation is now a generally accepted treatment for the management of a range of chronic, end-stage lung diseases, with evidence supporting quality of life and survival benefit for lung transplant recipients. Guidelines are based primarily on consensus of opinion rendered by experts in the field and on analysis of retrospective single-center and multicenter studies and registries.

The definitive work addressing criteria for selecting lung transplant patients, and contraindications against performing surgery, are written by the Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation (ISHLT). The ISHLT updated its consensus document on selection of lung transplant candidates in 2021 (Leard, 2021).

Coding

The following codes are included below for informational purposes only; inclusion of a code does not constitute or imply coverage or reimbursement.

Code	Description
32850	Donor pneumonectomy(s) (including cold preservation), from cadaver donor
32851	Lung transplant, single; without cardiopulmonary bypass
32852	Lung transplant, single; with cardiopulmonary bypass
32853	Lung transplant, double (bilateral sequential or en bloc); without cardiopulmonary bypass
32854	Lung transplant, double (bilateral sequential or en bloc); with cardiopulmonary bypass
32855	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
32856	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

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Policy history

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