Preauthorization is required and must be obtained through Case Management.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient’s contract at the time the services are rendered.

RELATED PROTOCOLS
Heart/Lung Transplant
Outpatient Pulmonary Rehabilitation

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DESCRIPTION
A lung transplant consists of replacing all or part of diseased lungs with healthy lung(s) or lobes. Transplantation is an option for patients with end-stage lung disease.

SUMMARY OF EVIDENCE
For individuals who have end-stage pulmonary disease who receive a lung transplant, the evidence includes case
series and registry studies. Relevant outcomes are overall survival (OS), change in disease status, and treatment-related mortality and morbidity. International registry data on a large number of patients receiving lung transplantation (>50,000) found relatively high patient survival rates, especially among those who survived the first year posttransplant. After adjusting for potential confounding factors, survival did not differ significantly after single- or double-lung transplant. Lung transplantation may be the only option for some patients with end-stage lung disease. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have end-stage pulmonary disease who receive a lobar lung transplant, the evidence includes case series and systematic reviews. Relevant outcomes are OS, change in disease status, and treatment-related mortality and morbidity. There are less data on lung lobar transplants than on whole-lung transplants, but several case series have reported reasonably similar survival outcomes between the procedures, and lung lobar transplants may be the only option for patients unable to wait for a whole-lung transplant. A 2017 systematic review found 1-year survival rates in available published studies ranging from 50% to 100%. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with a prior lung or lobar transplant and meet criteria for a lung transplant who receive a lung or lobar lung retransplant, the evidence includes case series and registry studies. Relevant outcomes are OS, change in disease status, and treatment-related mortality and morbidity. Data from registries and case series have found favorable outcomes with lung retransplantation in patients who meet criteria for initial lung transplantation. Given the exceedingly poor survival prognosis without retransplantation of patients who have exhausted other treatments, the evidence of a moderate level of posttransplant survival may be considered sufficient in this patient population. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

POLICY

Lung transplantation may be considered medically necessary for carefully selected patients with irreversible, progressively disabling, end-stage pulmonary disease unresponsive to maximum medical therapy (see Policy Guidelines).

A lobar lung transplant from a living or deceased donor may be considered medically necessary for carefully selected patients with end-stage pulmonary disease (see Policy Guidelines).

Lung or lobar lung retransplantation after a failed lung or lobar lung transplant may be considered medically necessary in patients who meet criteria for lung transplantation.

Lung or lobar lung transplantation is considered investigative in all other situations.

POLICY GUIDELINES

Individual transplant facilities may have their own additional requirements or protocols that must be met in order for the patient to be eligible for a transplant at their facility.

CONTRAINDICATIONS

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 disease not attributed to 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.

Policy specific
• Coronary artery disease not amenable to percutaneous intervention or bypass grafting, or associated with significant impairment of left ventricular function*; or
• Colonization with highly resistant or highly virulent bacteria, fungi, or mycobacteria.

*Some patients may be candidates for combined heart and lung transplantation. See the Heart/Lung Transplant Protocol.

Patients must meet United Network for Organ Sharing guidelines for a Lung Allocation Score (LAS) greater than zero.

LUNG-SPECIFIC GUIDELINES
Bilateral lung transplantation is typically required when chronic lung infection and disease is present (i.e., associated with cystic fibrosis and bronchiectasis). Some, but not all, cases of pulmonary hypertension will require bilateral lung transplantation.

Bronchiolitis obliterans is associated with chronic lung transplant rejection, and thus may be the etiology of a request for lung retransplantation.

MEDICARE ADVANTAGE
If a transplant is needed, we arrange to have the Medicare–approved transplant center review and decide whether the patient is an appropriate candidate for the transplant.

BACKGROUND
Solid organ transplantation offers a treatment option for patients with different types of endstage organ failure that can be lifesaving or provide significant improvements to a patient’s quality of life. 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 the Organ Procurement and Transplantation Network (OPTN) and United Network of Organ Sharing.

LUNG TRANSPLANT
In 2020, 39,036 transplants were performed in the United States procured from more than 12,500 deceased donors and 5,700 living donors. Lung transplants were the fourth most common procedure with 2,539 transplants performed from both deceased and living donors in 2020.

End-stage lung disease may derive from different etiologies. The most common indications for lung transplantation are chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, cystic fibrosis, α1-antitrypsin deficiency, and idiopathic pulmonary arterial hypertension. Before consideration for transplant, patients should be receiving maximal medical therapy, including oxygen supplementation, or surgical options, such as lung volume
reduction surgery for chronic obstructive pulmonary disease. Lung or lobar lung transplantation is an option for patients with end-stage lung disease despite these measures.

A lung transplant refers to single-lung or double-lung replacement. In a single-lung transplant, only 1 lung from a deceased donor is provided to the recipient. In a double-lung transplant, both the recipient’s lungs are removed and replaced by the donor’s lungs. In a lobar transplant, a lobe of the donor’s lung is excised, sized appropriately for the recipient’s thoracic dimensions, and transplanted. Donors for lobar transplant have primarily been living-related donors, with 1 lobe obtained from each of 2 donors (generally friends or family members) in cases for which bilateral transplantation is required. There are also cases of cadaver lobe transplants.

Potential recipients who are 12 years of age and older are ranked according to the Lung Allocation Score.3 A score may range between 0 and 100 and incorporates predicted survival after transplantation and predicted survival on the waiting list; the Lung Allocation Score takes into consideration the patient’s disease and clinical parameters. The waiting list incorporates the Lung Allocation Score, geography, and blood type classifications. Children younger than 12 years old receive a priority for lung allocation. Under this system, children younger than 12 years old with respiratory lung failure and/or pulmonary hypertension who meet criteria are considered “priority 1”, and all other candidates in the age group are considered “priority 2”. A lung review board has the authority to adjust scores on appeal for adults and children.

POTENTIAL CONTRAINDICATIONS TO TRANSPLANTATION

Malignancy

Malignancies are common after lung transplantation, with 21% and 40% of patients reporting 1 or more malignancies at 5 and 10 years posttransplantation, respectively.4 Skin cancer occurred most frequently, and lymphoproliferative disorders were the malignancies most associated with morbidity posttransplantation.

Human Immunodeficiency Virus Infection

Current OPTN policy permits human immunodeficiency virus (HIV)-positive transplant candidates. The 2020 US Public Health Service guideline also allows for transplantations in HIV-positive recipients with proper screenings and effective regimens for HIV infections.5

The British HIV Association and the British Transplantation Society (2017) updated their guidelines on kidney transplantation in patients with HIV disease.6 These criteria for adding a patient to the waitlist 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 Infections

Infection with *Burkholderia cenocepacia* is associated with increased mortality in some transplant centers, a factor that may be considered when evaluating the overall risk of transplant survival.7 Two articles have evaluated the impact of infection with various species of *Burkholderia* on outcomes for lung transplantation for cystic fibrosis. In a study by Murray et al (2008), multivariate Cox survival models were applied to 1026 lung transplant candidates and 528 transplant recipients.8 Of the transplant recipients, 88 were infected with *Burkholderia*. Among transplant recipients infected with *B. cenocepacia*, only those infected with nonepidemic strains (n=11) had significantly greater posttransplant mortality than uninfected patients (HR, 2.52; 95% CI, 1.04 to 6.12;
p=.04). Transplant recipients infected with *Burkholderia gladioli* (n=14) also had significantly greater posttransplant mortality than uninfected patients (HR, 2.23; 95% CI, 1.05 to 4.74; p=.04). When adjustments for specific species or strains were included, the Lung Allocation Scores of *Burkholderia multivorans*-infected transplant candidates were comparable with uninfected candidate scores, and scores for patients infected with nonepidemic *B. cenocepacia* or *B. gladioli* were lower. In a smaller study of 22 patients colonized with *Burkholderia cepacia* complex who underwent lung transplantation in 2 French centers, Boussaud et al (2008) reported that the risk of death by univariate analysis was significantly higher for the 8 patients infected with *B. cenocepacia* than for the other 14 colonized patients (11 of whom had *B. multivorans*).9

An analysis of international registry data by Yusen et al (2016) found that non-cytomegalovirus (CMV) infection is a major cause of mortality within 30 days of a lung transplant in adults.10 A total of 655 (19%) of 3424 deaths after transplants between 1990 and 2015 were due to non-CMV infection. Only 3 (0.1%) of the deaths were due to CMV infection.

**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.

Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary Services Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. *Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.*

**REFERENCES**

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.


