Lung and Lobar Lung Transplant

I. Description

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

End-stage lung disease may be the consequence of a number of different etiologies. The most common indications for lung transplantation are chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), cystic fibrosis (CF), alpha-1 antitrypsin deficiency, and idiopathic pulmonary arterial hypertension (IPAH). Prior to the consideration for transplant, patients should be receiving maximal medical therapy, including oxygen supplementation, or surgical options, such as lung-volume reduction surgery for COPD. 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 one 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 one lobe obtained from each of two donors (e.g., mother and father) in cases for which bilateral transplantation is required. There are also cases of cadaver lobe transplants. Combined lung-pancreatic islet cell transplant is being studied for patients with cystic fibrosis. (1)

Since 2005, potential recipients have been ranked according to the Lung Allocation Score (LAS). (2) Patients 12 years of age and older receive a score between 1 and 100 based on predicted survival after transplantation reduced by predicted survival on the waiting list; the LAS takes into consideration the patient’s disease and clinical parameters. In 2010, a simple priority system was implemented for children under the age of 12. Under this system, children under 12 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 (LRB) has authority to adjust scores on appeal for adults and children.

II. Policy

A. Lung transplantation is covered (subject to Administrative Guidelines) for carefully selected patients with irreversible, progressively disabling, end-stage pulmonary disease unresponsive to maximum medical therapy, including but not limited to one of the conditions listed below.

B. A lobar lung transplant from a living or deceased donor is covered (subject to Administrative Guidelines) for children and adolescents with end-stage pulmonary disease including but not limited to one of the conditions listed below.

- Bilateral bronchiectasis
- Alpha-1 antitrypsin deficiency
- Primary pulmonary hypertension
- Cystic fibrosis (both lungs to be transplanted)
- Bronchopulmonary dysplasia
- Postinflammatory pulmonary fibrosis
- Idiopathic/interstitial pulmonary fibrosis
- Sarcoidosis
- Scleroderma
- Lymphangiomymomatosis
- Emphysema
- Eosinophilic granuloma
- Bronchiolitis obliterans
- Recurrent pulmonary embolism
- Pulmonary hypertension due to cardiac disease
- Chronic obstructive pulmonary disease
- Eisenmenger’s syndrome

III. Policy Guidelines

General:

Potential contraindications subject to the judgment of the transplant center:

1. Known current malignancy, including metastatic cancer
2. Recent malignancy with high risk of recurrence
3. Untreated systemic infection making immunosuppression unsafe, including chronic infection
4. Other irreversible end-stage disease not attributed to lung disease
5. History of cancer with a moderate risk of recurrence
6. Systemic disease that could be exacerbated by immunosuppression
7. Psychosocial conditions or chemical dependency affecting ability to adhere to therapy
Policy Specific:
8. Coronary artery disease (CAD) not amenable to percutaneous intervention or bypass grafting, or associated with significant impairment of left ventricular function*; or
9. Colonization with highly resistant or highly virulent bacteria, fungi, or mycobacteria.

Patients must meet UNOS guidelines for lung allocation score (LAS) greater than zero.

Lung Specific
A. Bilateral lung transplantation is typically required when chronic lung infection disease is present, i.e., associated with cystic fibrosis and bronchiectasis. Some, but not all, cases of pulmonary hypertension will require bilateral lung transplantation.
B. Bronchiolitis obliterans is associated with chronic lung transplant rejection, and thus may be the etiology of a request for lung retransplantation.

IV. Administrative Guidelines
Precertification is required. To precertify, complete HMSA's Precertification Request and mail or fax the form as indicated along with the required documentation.

<table>
<thead>
<tr>
<th>Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>32850</td>
<td>Donor pneumonectomy(ies) (including cold preservation), from cadaver donor</td>
</tr>
<tr>
<td>32851</td>
<td>Lung transplant, single; without cardiopulmonary bypass</td>
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<tr>
<td>32852</td>
<td>with cardiopulmonary bypass</td>
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<tr>
<td>32853</td>
<td>Lung transplant, double (bilateral, sequential, or en bloc); without cardiopulmonary bypass</td>
</tr>
<tr>
<td>32854</td>
<td>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 tissues to prepare pulmonary venous/atrial cuff, pulmonary artery, and bronchus, unilateral</td>
</tr>
<tr>
<td>32856</td>
<td>bilateral</td>
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<tr>
<td>S2060</td>
<td>Lobar lung transplantation</td>
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<tr>
<td>S2061</td>
<td>Donor lobectomy (lung) for transplantation, living donor</td>
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V. Scientific Background

Literature Review

This policy was originally created in 1996 and updated regularly with searches of the MEDLINE database. The most recent literature search was performed for the period of October 2010 through October 2011. Due to the nature of the population, there are no randomized controlled trials (RCTs) that compare lung transplantation with alternatives. Systematic reviews are based on case series and registry data. The extant RCTs compare surgical technique, infection prophylaxis, or immunosuppressive therapy and are not germane to this policy. The following is a summary of the evidence based on registries, case series, and expert opinion.

Survival

The Registry of the International Society for Heart and Lung Transplantation (ISHLT) had reports from centers around the world of 3,272 lung transplants performed in 2009. (3) The overall median survival of patients who underwent lung transplantation between 1994 and June 2010 was 5.5 years. In the first 30 days after transplantation and the first year, the major reported causes of mortality were graft failure and non- cytomegalovirus (CMV) infections. Beyond the first year, the most common reported causes of mortality were bronchiolitis obliterans and non-CMV infections. Over time, the proportion of patients who died from malignancies increased; malignancies accounted for 15% of all deaths between 5 and 10 years after transplant. Authors of a 2009 review of the current status of lung transplantation observed that while transplantation can prolong survival, survival statistics for lung transplantation are not as favorable as in patients receiving other solid organ transplants. (4)

In 2009, Thabut and colleagues reported on a comparison of patients undergoing single- and double-lung transplantation for idiopathic pulmonary fibrosis (IPF). (5) A retrospective review was conducted of 3,327 patients with data in the UNOS registry. More patients underwent single-lung as compared to double-lung transplant (64.5 vs. 35.5%, respectively). Median survival time was greater for the double-lung group at 5.2 years (95% confidence interval [CI], 4.3 to 6.7 years) versus 3.8 years (95% CI, 3.6 to 4.1 years; p<0.001). After adjustment for baseline differences, however, survival times were not statistically different. The authors concluded that overall survival did not differ between the 2 groups: single-lung transplants offered improved short-term survival but long-term harm, whereas double-lung transplant increased short-term harm but was associated with a long-term survival benefit.

Patient Selection

In 2008, Kozower and colleagues performed a retrospective cohort study using data from 5 academic medical centers to evaluate the impact of a new lung allocation score on short-term outcomes after lung transplantation. (6) (This lung allocation score was implemented in May 2005 by the Organ Procurement and Transplantation Network [OPTN].) This new score changed lung allocation from a system based on waiting time to an algorithm based on the probability of survival for 1 year on the transplant list and survival 1-year post-transplantation. Results were compared for 170 patients who received transplants on the basis of the new lung allocation scores (May 4,
2005 to May 3, 2006) with those of 171 patients who underwent transplants the preceding year before implementation of the scoring system. Waiting time decreased from 681 to 445.6 days (p<0.001). Recipient diagnoses changed, with an increase (15% to 25%) in idiopathic pulmonary fibrosis cases and decreases in emphysema (46% to 34%) and cystic fibrosis (CF) (23% to 13%). Hospital mortality and 1-year survival were the same between groups (5.3% vs. 5.3% and 90% vs. 89%, respectively). Presumably due to increased severity of illness, the incidence of primary graft dysfunction and postoperative intensive care unit length of stay increased in the year after implementation of the scoring system; graft dysfunction grew from 14.8% (24/170) to 22.9% (39/171); (p=0.04) and length of stay rose from 5.7 to 7.8 days.

In 2010, Yusen and colleagues reviewed the effect of the Lung Allocation Score (LAS) on lung transplantation by comparing statistics for the period before and after its implementation in 2005. (7) Other independent changes in clinical practice, which may affect outcomes over the same period of time, include variation in immunosuppressive regimens, an increased supply of donor lungs, changes in diagnostic mix, and increased consideration of older recipients. Deaths on the waiting list declined following implementation of the LAS system, from approximately 500 per 5,000 patients to 300 per 5,000 patients. However, it is expected that implementation of the LAS affected patient characteristics of transplant applicants. One-year survival post-transplantation did not improve after implementation of the LAS system: patient survival data before and after are approximately 83%. Long-term survival data are not yet available for comparison.

**Pediatric Considerations**

In 2011, Benden and colleagues reviewed pediatric lung transplants that have been reported to the international registry. (8) Pediatric patients are defined as those younger than 18 years of age. The authors noted an increase in the number of pediatric lung transplants in recent years; there were 127 transplants in 2009 compared to 73 in 1999. In contrast to adult patients, the most common indication for pediatric patients was cystic fibrosis, accounting for 56% of lung transplants in 6-11 year-olds and 72% of lung transplants in 12-17 year-olds that occurred between 1990 and June 2010. Survival has improved in the recent era, and 5-year survival is equivalent to adult recipients. For children receiving allografts between 2002 and June 2009, the 5-year survival rate was 53% and the 7-year survival rate was 45%. Patients aged 1 to 11 years had a significantly better survival rate than those between the ages of 12 and 17 years. In the first year after lung transplantation, non-CMV infection and graft failure were the 2 leading causes of death.

**Contraindications**

**Malignancy**

Concerns regarding a potential recipient’s history of cancer have been based on the observation of significantly increased incidence of cancer in kidney transplant patients. (9) For renal transplant patients who had a malignancy treated prior to transplant, the incidence of recurrence ranged from zero to more than 25%, depending on the tumor type. (10,11) However, it should be noted that the availability of alternative treatment strategies informs recommendations for a waiting period following high-risk malignancies: in renal transplant, a delay in transplantation is possible due to dialysis; end-stage lung disease patients may not have an option to defer.
**HIV**

Solid organ transplant for patients who are human immunodeficiency virus (HIV)-positive has been controversial, due to the long-term prognosis for HIV positivity and the impact of immunosuppression on HIV disease. Although HIV-positive transplant recipients may be of research interest at some transplant centers, the minimal data regarding long-term outcome in these patients primarily consist of case reports and abstract presentations of liver and kidney recipients. Nevertheless, some transplant surgeons would argue that HIV positivity is no longer an absolute contraindication to transplant due to the advent of highly active antiretroviral therapy (HAART), which has markedly changed the natural history of the disease.

In March 2009, the Organ Procurement Transplantation Network (OPTN) revised its policies on HIV status in recipients. It reiterates an earlier position that: “A potential candidate for organ transplantation whose test for HIV is positive but who is in an asymptomatic state should not necessarily be excluded from candidacy for organ transplantation, but should be advised that he or she may be at increased risk of morbidity and mortality because of immunosuppressive therapy.” (12)

In 2006, the British HIV Association and the British Transplantation Society Standards Committee published guidelines for kidney transplantation in patients with HIV disease. (13) These criteria may be extrapolated to other organs:

- **CD4 count greater than 200 cells/ml for at least 6 months**
- **Undetectable HIV viremia (less than 50 HIV-1 RNA copies/ml) for at least 6 months**
- **Demonstrable adherence and a stable HAART regimen for at least 6 months**
- **Absence of AIDS defining illness following successful immune reconstitution after HAART.**

**Other Infections**

Infection with B cenocepacia is associated with increased mortality in some transplant centers, a factor that may be taken into account when evaluating overall risk for transplant survival. (14) Two papers published in 2008 evaluated the impact of infection with various species of Burkholderia on outcomes for lung transplantation for CF. Murray and colleagues sought to quantify the risks of infection with Burkholderia species on survival before and after transplantation. (15) Multivariate Cox survival models assessing hazard ratios (HRs) were applied to 1,026 lung transplant candidates and 528 transplant recipients. Of the transplant recipients, 88 were infected with Burkholderia. Among transplant recipients infected with Burkholderia cenocepacia, only those infected with nonepidemic strains (n=11) had significantly greater post-transplant mortality than uninfected patients (HR, 2.52; 95% confidence interval [CI, 1.04-6.12; p=0.04). Transplant recipients infected with Burkholderia gladioli (n=14) also had significantly greater post-transplant mortality than uninfected patients (HR, 2.23; 95% CI, 1.05-4.74; p=0.04). Hazard ratios for patients infected with Burkholderia multivorans (n=32) were similar to those for uninfected transplant recipients (HR, 0.66). When adjustments for specific species/strains were included, lung allocation scores of B multivorans-infected transplant candidates were comparable to uninfected candidate scores, and scores for patients infected with non-epidemic B cenocepacia or B gladioli were lower. In a smaller
study of 22 patients colonized with Burkholderia cepacia complex who underwent lung transplantation in two French centers, 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). (16)

Patients colonized with pan-resistant bacteria other than B cepacia appear to have slightly decreased survival relative to patients harboring sensitive bacteria. In a retrospective report with 103 patients, survival with pan-resistant bacteria was 91% at 1 year, 89% at 2 years, 63% at 3 years, and 58% at 5 years; this was compared to survival rates of patients with sensitive bacteria (98%, 97%, 91%, and 85%, respectively) from the same centers, and to survival rates for patients with CF from the UNOS registry (1 year, 86%; 3 years, 65%; 5 years, 50%). (17)

Pinney and colleagues published a retrospective review of invasive fungal infection rates in lung transplantation patients without CF treated at a single center. (18) Patients were followed for a median of 34 months. Invasive fungal infections were identified in 22 of 242 (9.1%) patients. Aspergillus infections were most common, occurring in 11 of 242 (4.5%) of patients. There were also 7 cases (3%) of Candida infection. Survival rates did not differ significantly in patients with invasive fungal infections compared to the entire cohort of patients. For example, 3-year survival was 50% among patients with invasive fungal infection and 66% in the entire cohort, p=0.66. The authors did not compare survival in patients with invasive fungal infections to survival only in those without invasive fungal infections.

**Coronary Artery Disease (CAD)**

In 2011, Sherman and colleagues reported on outcomes in 27 patients with CAD at a single center who underwent lung transplantation and coronary revascularization. (19) Patients needed to be otherwise considered good candidates for transplantation and have discrete coronary lesions (at least 50% in the left main artery or at least 70% in other major vessels) and preserved ejection fraction. Thirteen patients had single-lung transplantation and 14 had double-lung transplantation. Outcomes were compared with a control group of 81 patients without CAD who underwent lung transplantation; patients were matched for age, diagnosis, lung allocation score and type of procedure. During a mean follow-up of 3 years, 9 of 27 (33%) patients with CAD and 28 of 81 (35%) without CAD died, p=0.91. Bronchiolitis obliterans and infection were the primary causes of death. There was no significant difference between groups in a composite outcome of adverse cardiac events (defined as acute coronary syndrome, redo revascularization or hospital admissions for congestive heart failure), p=0.80.

**Summary**

The literature on lung transplantation, which consists of case series and registry data, demonstrates that lung transplantation provides a survival benefit in appropriately selected patients and thus may be considered medically necessary. It may be the only option for some patients with end-stage lung disease.
Technology Assessments, Guidelines, and Position Statements

In 2006, the Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation published consensus-based guidelines on selection of lung transplant candidates (20) The guidelines state that, “Lung transplantation is now a generally accepted therapy 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 requirement of one potential recipient against those of others in their society. These concepts apply equally to listing a candidate with the intention to transplant and potentially de-listing (perhaps only temporarily) a candidate whose health condition changes such that a successful outcome is no longer predicted.”

Medicare National Coverage

Lung transplantation is covered under Medicare when performed in a facility that is approved by Medicare as meeting institutional coverage criteria—approximately 57 programs in the U.S. (21) The Centers for Medicare and Medicaid Services have stated that under certain limited cases, exceptions to the facility-related criteria may be warranted if there is justification and the facility ensures safety and efficacy objectives.

VI. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.
VII. References


