7.01.128	Endobronchial Valves		
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Policy Statement

Endobronchial valves are considered **investigational** in **all** situations including, but not limited to:

- Treatment of prolonged air leaks
- Treatment for patients with chronic obstructive pulmonary disease or emphysema

Policy Guidelines

The IBV® Valve System (Spiration Inc., Redmond, WA) is the only endobronchial valve device that has approval from the U.S. Food and Drug Administration (FDA) through the Humanitarian Device Exemption (HDE) process for use in prolonged pulmonary air leaks. In accordance with the FDA HDE guidelines, before the device can be used in a patient, the physician must obtain approval from the HDE-holder, the Institutional Review Board (IRB) of the health care facility, and the FDA.

The use of endobronchial valves as a treatment of prolonged air leaks may be reviewed on a case by case basis, when FDA HDE parameters for the device have been met and approval has been attained by the HDE-holder, IRB, and the FDA.

Coding

The following CPT codes are specific for this procedure:

- **31647**: Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with balloon occlusion, when performed, assessment of air leak, airway sizing, and insertion of bronchial valve(s), initial lobe
- **31651**: Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with balloon occlusion, when performed, assessment of air leak, airway sizing, and insertion of bronchial valve(s), each additional lobe (List separately in addition to code for primary procedure[s])
- **31648**: Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with removal of bronchial valve(s), initial lobe
- **31649**: Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with removal of bronchial valve(s), each additional lobe (List separately in addition to code for primary procedure)

Description

Endobronchial valves are synthetic devices that are deployed with bronchoscopy into ventilatory airways of the lung for the purpose of controlling airflow. They have been investigated for use in patients who have prolonged bronchopleural air leaks, as well as an alternative to lung volume reduction surgery in patients with lobar hyperinflation from severe or advanced emphysema.

Related Policies

- Lung Volume Reduction Surgery for Severe Emphysema

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the

contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates [e.g., Federal Employee Program (FEP)] prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

In October 2008, the IBV® Valve System (Spiration, Redmond, WA) was approved by the U.S. Food and Drug Administration (FDA) under the humanitarian device exemption process for use in controlling prolonged air leaks of the lung or significant air leaks that are likely to become prolonged air leaks following lobectomy, segmentectomy, or lung volume reduction surgery. An air leak present on postoperative day 7 is considered prolonged unless present only during forced exhalation or cough. An air leak present on day 5 should be considered for treatment if it is: (1) continuous, (2) present during normal inhalation phase of inspiration, or (3) present on normal expiration and accompanied by subcutaneous emphysema or respiratory compromise. IBV Valve System use is limited to 6 weeks per prolonged air leak. FDA product code: OAZ.

In December 2008, the Zephyr® Endobronchial Valve (formerly Emphasys, now Pulmonx, Redwood City, CA) was considered by the Anesthesiology and Respiratory Therapy Device Panel for use as a permanent implant intended to improve forced air expiratory volume in 1 second and 6-minute walk test distance in patients with severe, heterogeneous emphysema who have received optimal medical management. The panel declined to recommend the device for FDA approval. As of June 2016, the Zephyr Endobronchial Valve has not been approved by the FDA.

Rationale

Background
Proper lung functioning depends on separation between the air-containing parts of the lung and the small vacuum-containing space around the lung called the pleural space. When air leaks into the pleural space, the lung is unable to inflate, resulting in hypoventilation and hypoxemia; this condition is known as a pneumothorax. A pneumothorax can result from trauma, high airway pressures induced during mechanical ventilation, lung surgery, and rupture of lung blebs or bullae, which may be congenital or a result of chronic obstructive pulmonary disease (COPD).

Although an air leak from the lung into the pleural space may seal spontaneously, it often requires intervention. Techniques currently employed to close air leaks include the following:

- Inserting a chest tube (tube thoracostomy) and employing a water seal or 1-way valve to evacuate air collected in the pleural space and prevent it from reaccumulating
- Lowering airway pressures by adjusting the mechanical ventilator
- Using autologous blood patches
- Performing a thoracotomy with mechanical or chemical pleurodesis

An endobronchial valve is a device that permits 1-way air movement. During inhalation, the valve is closed, preventing air flow to the diseased area of the lung. The valve opens during exhalation to allow air to escape from the diseased area of the lung. When used to treat persistent air leak from the lung into the pleural space, the endobronchial valve theoretically permits less air flow across the diseased portion of the lung during inhalation, aiding in air leak closure. The valve may be placed, and subsequently removed, by bronchoscopy.

Endobronchial valves have also been investigated for use in severe emphysematous COPD. In emphysematous COPD, peripheral lung tissue may form bullae. These diseased portions of the lung ventilate poorly, cause air trapping, and hyperinflate, compressing relatively normal lung tissue. They also may rupture, causing a pneumothorax. Use of an endobronchial valve is thought to prevent hyperinflation of these bullae.

Use of endobronchial valves in COPD is based on the improvement observed in patients who have undergone lung volume reduction surgery (LVRS). LVRS involves excision of peripheral emphysematous lung tissue, generally from the upper lobes. The precise mechanism of clinical improvement for patients undergoing lung volume reduction has not been firmly established. However, it is believed that elastic recoil and diaphragmatic function are improved by reducing the volume of diseased lung. The procedure is designed to relieve dyspnea and improve functional lung capacity and quality of life; it is not curative. Endobronchial valves have been investigated as a nonsurgical alternative to LVRS.

Literature Review

Treatment of Air Leaks

No randomized controlled trials (RCTs) or comparative observational studies were identified. Only case series and case reports are available. The largest case series, published in 2009, reported on 40 patients treated at 17 sites in the United States and Europe; 6 of the patients had been included in previously published case reports.[1] Zephyr endobronchial valves were used. Data were abstracted retrospectively from medical records. No specific eligibility criteria were reported, and patients did not need to demonstrate that they were refractory to other treatments. All patients in the series had prolonged pulmonary air leak (mean duration, 119 days; median, 20 days). Twenty-five patients had continuous air leaks, 14 had expiratory air leaks, and 1 was unidentified. The most common comorbidities were cancer and chronic obstructive pulmonary disease (COPD). Prior to surgery, 39 of the 40 patients had had at least 1 chest tube. Five patients had also had other treatments (e.g., blood patch before valve placement). The mean (SD) number of valves placed per patient was 2.9 (1.9). After valve placement, 19 (47.5%) patients had complete resolution of acute air leak, 18 (45%) had a reduction in air leak, 2 (5%) had no change, and no data were available for 1 patient. The mean time from valve placement to chest tube removal was 21 days (median time, 7.5 days; data from 2 patients not available). Eight patients had the valves removed after the air leak ceased; in 32 patients, the clinician chose to leave the valves in place. Six patients experienced adverse effects related to valve placement including valve expectoration, moderate oxygen desaturation, initial malpositioning of a valve, pneumonia, and *Staphylococcus aureus* colonization. The length of follow-up varied, ranging from 5 to 1109 days. At last follow-up, 16 patients had died, though none of the deaths were attributed to the valve or the implantation procedure.

The next largest case series is the 2013 study by Firlinger et al in Austria.[2] The study included 16 patients with persistent continuous air leak (i.e., having an intrathoracic chest tube for >7 days despite conservative and/or surgical therapy). Endobronchial valves were placed in 13 of 16 patients, but not in the other 3 who had intermittent air leaks U.S. Food and Drug Administration (FDA)-approved Spiration IBV valves were used in 9 patients and Zephyr valves in the other 4 patients. Ten (77%) of 13 patients were considered responders, defined as successful chest tube removal without need for further intervention. Spiration IBV valves were used in 6 of 10 responders and all 3 nonresponders.

In addition, a 2011 case series reported on 9 patients with pulmonary air leaks evaluated for treatment with Spiration IBV valves.[3] Target airways could not be identified in 2 patients; valves were placed in 7 patients. One of the 7 had 2 procedures due to development of an additional air leak after the first was treated and resolved. The median duration of air leaks in the 7 patients before valve placement was 4 weeks (range, 2 weeks to 5 months). Complete air leak cessation occurred in 6 of 8 procedures after a mean duration of 5.2 days. The other 2 procedures resulted in reduction of air leak. There were no operative or postoperative complications attributed to

the bronchial valves. The valves were removed in 5 of the 7 patients at a mean of 37 days after placement (range, 14-55 days). Valves were not removed in 1 patient who entered hospice care and in the patient who underwent 2 procedures because the patient declined removal.

Section Summary: Treatment of Air Leaks
The only available data on endobronchial valves for treating persistent air leaks are uncontrolled trials with small numbers of heterogeneous patients. Data on FDA-approved endobronchial valve device are particularly limited; Spiration valves were successfully placed in 7 patients in 1 case series and 9 patients in another. This evidence is not adequate to determine the impact of this technology on the net health outcome, nor does it provide any comparative data with alternatives.

Treatment of Severe and Advanced Emphysema
Three RCTs have evaluated the safety and efficacy of endobronchial valves as a treatment of emphysema. Two trials were multicenter and industry-sponsored. One trial used the Zephyr valve, which is not FDA-approved, and the other used the IBV valve. The third RCT was a single-center study of the Zephyr valve funded by a government grant from the U.K.

Randomized Controlled Trials
Endobronchial Valve for Emphysema Palliation Trial
The Endobronchial Valve for Emphysema Palliation Trial (VENT) was randomized but not blinded. Primary results were published by Sciurba et al (U.S. cohort)[4] and Herth et al (European cohort).[5] Key eligibility criteria for participation were: diagnosis of heterogeneous emphysema, forced air expiratory volume in 1 second (FEV_1) of 15% to 45% of the predicted value, total lung capacity of more than 100% of predicted value, residual volume of more than 150% of predicted value, and postrehabilitation 6-minute walk test (6MWT) distance of at least 140 meters. Before randomization, all patients received 6 to 8 weeks of pulmonary rehabilitation and medical management optimized at the discretion of the treating physician, using guidelines from the Global Initiative for Chronic Obstructive Lung Disease (GOLD). Patients who remained eligible for the trial after undergoing the preliminary treatment program were randomized to receive therapy using the Zephyr endobronchial valve or standard care. Patients were followed for 12 months and primary outcomes were reported after 6 months. The primary effectiveness outcomes were percent change from baseline to 6 months in the FEV_1 and distance on the 6MWT. Primary results from the 31 U.S. sites were reported in 2010; results from the 23 sites in Europe were reported in 2012. Pooled 6-month outcomes from both cohorts were reported in 2013. A limitation of the trial design was lack of blinding, which could have affected performance on the primary efficacy outcomes (e.g., it may have affected clinicians' coaching of patients and/or the degree of effort exerted by patients).

U.S. Cohort Findings
As reported by Sciurba et al, 321 patients in the United States were randomly assigned on a 2:1 basis to receive Zephyr endobronchial valves (n=220) or standard medical care (n=101).[4] The mean number of valves placed in the endobronchial valve group was 3.8 per patient (range, 1-9). A total of 42 (19.1%) of 220 patients in the endobronchial valve group and 28 (27.7%) of 101 in the control group had missing data for the primary efficacy outcomes. Most missing data was due to lack of compliance rather than death or illness. Although there was a prespecified plan for handling missing data, with this degree of data missing, findings might not accurately represent outcomes in the population. The data analysis was intention-to-treat and missing data were imputed. Primary outcome data at 6 months are listed in Table 1.

Table 1: Primary Outcomes Data at 6 Months in the U.S. Cohort

Outcomes	Endobronchial Valve Group (n=220)	Control Group (n=101)	Between-Group Difference, p Value
FEV_1			
Mean ABC from baseline (95% CI)	4.3% (1.4% to 7.2%)	-2.5% (-5.4% to 0.4%)	6.8% (2.1% to 11.5%), 0.005

Outcomes	Endobronchial Valve Group (n=220)	Control Group (n=101)	Between-Group Difference, p Value
Distance on 6-minute walk test			
Median change from baseline (95% CI), m	9.3 (-0.5 to 19.1)	-10.7 (-29.6 to 8.1)	19.1 (1.3 to 36.8), 0.02
Median ABC from baseline (95% CI)	2.5% (-1.1% to 6.1%)	-3.2% (-8.9% to 2.4%)	5.8% (0.5% to 11.2%), 0.04

ABC: absolute percent change; CI: confidence interval; FEV_1: forced air expiratory volume in 1 second.

Among the secondary outcomes reported at the 6-month follow-up, quality of life was measured using the St. George's Respiratory Questionnaire (SGRQ), which ranges from 0 to 100, with a higher score indicating a worse quality of life. At 6 months, the SGRQ score decreased by -2.8 points (95% confidence interval [CI], -4.7 to -1.0) in the endobronchial valve group and increased by 0.6 points (95% CI, -1.8 to 3.0) in the control group. The between-group difference was -3.4 (95% CI, -6.7 to 0.2), which was statistically significant (p=0.04) but was less than the 4-point change generally considered to represent a clinically meaningful difference.[6] According to body plethysmography, the mean (SD) change in total lung volume at 6 months was -1.2% (10.6%) in the endobronchial valve group and -0.4% (13.0%) in the control group; this difference was not statistically significant (p=0.41). Similarly, changes between groups in residual volume and inspiratory capacity were not statistically significant.

The primary safety variable was a composite measure consisting of 6 major complications (death, empyema, massive hemoptysis, pneumonia distal to valves, pneumothorax or air leak of >7 days in duration, ventilator-dependent respiratory failure for >24 hours). Complication rates by 6 months were 6.1% in the endobronchial group and 1.2% in the control group. The between-group difference was 4.9% (95% CI, 1.0 to 8.8), which was not statistically significant (p=0.08) and fell within the prespecified safety criteria. Adverse events to 6 months included 6 (2.8%) deaths in the endobronchial valve group and no deaths in the control group (p=0.19). Between 3 months and 12 months, 25 (11.7%) of 214 patients in the endobronchial valve group followed had experienced COPD exacerbations; 22 of these events resulted in hospitalization. Over the same time period, 8 (9.2%) of 87 patients in the control group had COPD exacerbations, all of which resulted in hospitalization. The difference in number of exacerbations was not statistically significant. For hemoptysis (other than massive) between 3 months and 12 months, there were 13 (6.1%) cases in the endobronchial valve group and none in the control group (p=0.02). Among the 214 patients who received valves and were followed to 12 months, there were 6 (2.8%) cases of valve expectoration, aspiration, or migration and 9 (4.2%) cases of bronchial granulation tissue. Valves were removed in 31 (14%) patients after 1 to 377 days; removal was based on investigators' discretion (there was no specific protocol).

European Cohort Findings
Herth et al reported on 171 patients in the European cohort of VENT; 111 patients were randomized to the endobronchial valve group and 60 patients to the standard care group.[5] During the trial, 10 patients died and 4 patients withdrew. The number of patients who were lost to follow-up or missing a visit was 12 at 6 months and 21 at 12 months. A total of 154 (90%) of 171 patients completed the 6-month follow-up and 136 (80%) of 171 completed the 12-month follow-up. Primary outcome data at 6 months in the European cohort are in Table 2 (outcome reporting differed slightly from the U.S. cohort).

Table 2: Primary Outcomes Data at 6 Months in the European Cohort

Outcomes	Endobronchial Valve Group (n=220)	Control Group (n=101)	P Value for Between-Group Difference
Forced air expiratory volume in 1 second			
Mean (SD) ABC from baseline	7% (20%)	0.5% (19%)	0.067
Distance on 6-minute walk test			
Median (SD) change from baseline, m	15 (91)	10 (78)	0.070

Outcomes	Endobronchial Valve Group (n=220)	Control Group (n=101)	P Value for Between-Group Difference
Mean (SD) change in cycle ergometry workload from baseline, W	2 (14)	-3 (10)	0.04

ABC: absolute percent change.

At 12 months, mean (SD) change in FEV_1 was 6 (26) in the endobronchial valve group and -2 (20) in the control group (p=0.05). The mean (SD) change in cycle ergometry workload was 1 (13) watt in the endobronchial valve group and -5 (12) watts in the control group (p=0.03). Data on the 6MWT distance at 12 months were not reported. Twenty percent of randomized patients did not provide data at 12 months.

Findings on the composite safety variable, reported for the U.S. cohort, were not reported for the European cohort. Herth reported that serious complications and rates of COPD exacerbations in the European cohort did not differ significantly between groups, and there were no reported cases of emphysema or massive hemoptysis. Five cases of pneumothorax requiring hospitalization for more than 7 days were reported in the endobronchial valve group. There were 10 deaths, 6 in the endobronchial valve group and 4 in the control group; none were considered to be related to study procedures. Over the 12-month follow-up, there were 13 cases of valve expectoration, aspiration or migration; this represented 13 (12%) of the 111 patients in the endobronchial valve group. Eight of 13 events occurred in the first 90 days after valve placement.

Pooled Cohort Data
Data from 416 (84.6%) of the 492 patients randomized in both cohorts who received follow-up computed tomography (CT) scans at 6 months were reported by Valipour et al (2014).[7] Of the 416 patients, 284 were in the endobronchial valve group and 132 were in the control group. The authors reported on several outcomes using an intention-to-treat approach; these outcomes were not listed as either primary or secondary outcome measures in the Sciurba report.[4] At 6 months, the mean target lobar volume reduction was significantly higher in patients receiving endobronchial valve therapy (EBV; -242 mL) than in control patients (0.5 mL; p<0.001). Moreover, 42% of patients in the EBV group and 24.7% of controls had improvement of at least 1 point in the Body Mass Index – Obstruction Metric – Dyspnea Score – Exercise Tolerance Composite (BODE) index at 6 months (p<0.001). (The BODE index combines several variables, including the FEV_1 and 6MWT distance). A higher score on the BODE index has been correlated with an increased risk of death from COPD.) Valipour did not discuss missing data on the FEV_1 or 6MWT measures at 6 months.

Bronchoscopic Lung Volume Reduction With Endobronchial Valves Reduces Dynamic Hyperinflation Trial
The Bronchoscopic Lung Volume Reduction With Endobronchial Valves Reduces Dynamic Hyperinflation (BeLieVeR-HIFi) trial, a government-funded study, evaluated the Zephyr endobronchial valve in a double-blind sham-controlled trial of 50 patients with heterogeneous emphysema and intact interlobar fissures.[8] The patient population was based on the subgroup analysis of VENT, which showed greater efficacy of endobronchial valves in patients with these characteristics. Included were patients with FEV_1 of less than 50% of predicted, significant hyperinflation, a restricted exercise capacity, and substantial breathlessness. The minimum clinically important differences were prespecified as a 15% increase for FEV_1 (primary outcome), a 350-mL reduction in the residual volume, a 4-point decrease in SGRQ score, a 2-point decrease on the COPD Assessment Test (CAT) score, a 105-second increase in endurance cycle time, and an 26-meter increase in 6MWT distance. Patients were randomized 1:1 to bronchoscopy plus valve placement or to bronchoscopy with sham valve placement. Valve placement led to statistically significant improvements in response rates for some outcomes compared to patients who underwent the sham procedure. Statistically significant differences in response rates were observed for FEV_1, 6MWT distance, and endurance cycle time, but not

residual volume, SGRQ score, or CAT score (see Table 3). Two patients in the bronchoscopy plus valve placement group died within 90 days of the procedure, 2 had pneumothoraces, and 4 patients expectorated a valve before 3 months.

Table 3: Three-Month Response Rates for the BeLieVeR-HIFi Trial

Outcome	Endobronchial Valve Group (n=25)	Control Group (n=25)	P Value for Between-Group Difference
Forced air expiratory volume in 1 second	39%	4%	0.004
Residual volume	48%	29%	0.24
Six-minute walk distance	52%	17%	0.012
Endurance cycle time	43%	8%	0.008
SGRQ score	48%	46%	1.0
CAT score	57%	29%	0.08

CAT: COPD Assessment Test; SGRQ: St. George's Respiratory Questionnaire.

IBV Valve Trial

The IBV Valve Trial, published by Wood et al (2014), was randomized and double-blind.[9] Key eligibility criteria for participation were: age 40 to 74 years, diagnosis of emphysema with severe dyspnea, and no more than 2 hospitalizations for COPD exacerbation or respiratory infection within the past year. Medical management was optimized before study participation, and patients eligible for LVRS or lung transplant received surgical counseling. All study participants underwent anesthesia for bronchoscopy and were then randomized on a 1:1 basis to active treatment (placement of IBV Valves) or sham treatment (no valve placement). Patients were assessed at 1, 3, and 6 months. The primary effectiveness outcome was a composite measure including change in disease-related quality of life, as defined by the SGRQ score. A reduction in SGRQ total score of at least 4 points from baseline was considered a clinically meaningful improvement. The composite measure also included change in lobar lung volume measured by quantitative CT. The CT threshold was at least a 10% increase in non-upper-lobe volume and any decrease in upper-lobe volume. The primary safety measure was the difference between groups in the number of serious adverse events.

The trial used an adaptive design with Bayesian statistical methodology. Subject recruitment was planned to stop if prespecified criteria involving Bayesian predictive probabilities were met; potential sample sizes ranged from 200 to 500. In actuality, 277 patients were randomized at 36 sites, 142 to the treatment group and 135 to the control group. A total of 121 (85%) patients in the treatment group and 134 (99%) in the control group completed the 6-month follow-up visit.

As shown in Table 4, 5% of patients in the treatment group and 0.7% in the control group were considered responders. According to Bayesian analysis, the posterior probability superiority in the treatment group was 97%, which exceeded the prespecified success of 95%. However, despite this statistical finding, the authors stated that the response rate in the treatment group was so low that it could not be considered a clinically meaningful finding.

Table 4: Composite Effectiveness Measure and Individual Components

Outcome	Treatment Group (n=142)	Control Group (n=135)	Difference (Treatment – Control), 95% BCrI
Composite measure			
No. of responders (%)	6/121 (5.0%)	1/134 (0.7%)	0.048%, 9.212%[a]
SGRQ score			
No. of responders (≥ -4 points, %)	39/121 (32.3%)	53/133 (39.8%)	-19.9%, 4.2%
Computed tomography volume, mL			
Mean upper-lobe change (SD)	-224 (299)	-17 (204)	-272, -14[a]
Mean non-upper-lobe change (SD)	214 (384)	-27 (292)	155, 326[a]

BCrI: Bayesian credible interval; SGRQ: St. George's Respiratory Questionnaire.
[a] Statistically significant.

In terms of safety, significantly more patients had a serious adverse event in the treatment group (n=20 [14%]) than the control group (n=5 [3.7%]). The most frequent event was COPD exacerbations (7 in the treatment group, 4 in the control group). Six patients in the treatment group and 1 in the control group died; none of the deaths were considered device-related. Pneumothorax, a device-related event, occurred in 3 (2.1%) patients, all in the treatment group.

Section Summary: Treatment of Severe and Advanced Emphysema
For patients with severe or advanced emphysema, the 3 published RCTs provide insufficient evidence that the technology improves the net health outcome. VENT was limited by a lack of blinding and a large amount of missing data. Also, in VENT, findings for primary outcomes were mixed; there was a statistically significant change in FEV_1 and in the 6MWT distance from baseline to 6 months in the U.S. cohort but not in the European cohort; there was a statistically significant change in FEV_1 at 12 months in the European cohort. For pooled trial data, the magnitudes of the primary outcomes that were statistically significant represented uncertain clinical significance. Results from the sham-controlled BeLieVeR-HIFi trial were mixed, with significant differences in response rates for FEV_1, 6MWT distance, and endurance cycle time, but not for residual volume, SGRQ score, or CAT score. Authors of the sham-controlled IBV Valve Trial concluded its study findings did not indicate a clinically meaningful benefit of endobronchial valves for patients with severe emphysema. In addition, across the 3 trials, patients who received endobronchial valves experienced numerous adverse events. In the BeLieVeR-HIFi trial, 1 of 25 patients died as a complication of valve removal, 2 had pneumothoraces, and 4 patients expectorated a valve before 3 months. In the IVB Valve Trial, the rate of serious adverse events was significantly higher in the treatment group than in the sham control group.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 5.

Table 5. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01812447[a]	A Prospective, Randomized, Controlled Multicenter Clinical Study to Evaluate the Safety and Effectiveness of the Spiration® Valve System for the Single Lobe Treatment of Severe Emphysema (EMPROVE)	270	Sep 2016
NCT01989182[a]	The Spiration Valve System for the Treatment of Severe Emphysema (SVS)	100	Sep 2016
NCT02382614[a]	Safety and Effectiveness of the Spiration Valve System (SVS) in Air Leaks (VAST)	200	Dec 2016
NCT02022683[a]	A Multi-center, Prospective, Randomized, Controlled Trial of Endobronchial Valve Therapy vs. Standard of Care in Heterogeneous Emphysema (TRANSFORM)	78	Feb 2018
NCT01796392[a]	Lung Function Improvement After Bronchoscopic Lung Volume Reduction With Pulmonx Endobronchial Valves Used in Treatment of Emphysema (LIBERATE)	183	Dec 2020

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

Summary of Evidence
For individuals who have pulmonary air leaks who receive endobronchial valves, the evidence includes case series. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, and treatment-related morbidity. The only available data on endobronchial valves for treating persistent air leaks are uncontrolled trials with small numbers of heterogeneous patients. Data on the Spiration™ endobronchial valve device (the only device approved by the U.S. Food and Drug Administration [FDA]) are particularly limited. These valves were successfully placed in 7 patients in 1 case series and in 9 patients in another series. These case series do not

provide any evidence on comparisons with alternatives. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have severe or advanced emphysema who receive endobronchial valves, the evidence includes 3 randomized controlled trials (RCTs). Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, and treatment-related morbidity. Of the 3 RCTs, 1 was unblinded and 2 did not use FDA-approved valves. Although some outcomes were statistically significant in favor of endobronchial valve treatment, the magnitude of the difference was generally of uncertain clinical significance. Moreover, the numerous adverse events experienced by patients who received endobronchial valves in these trials raise concerns about treatment safety. Overall, it is not possible to determine whether there is a clinically meaningful benefit. The evidence is insufficient to determine the effects of the technology on health outcomes.

Supplemental Information

Clinical Input Received From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests from Blue Cross Blue Shield Association, input was received through 1 physician specialty society and 3 academic medical centers in 2011. Those providing input generally agreed that use of endobronchial valves is investigational for treating emphysema. Regarding use of endobronchial valves for treating prolonged air leaks, reviewers acknowledged that only limited case series are available. Of the 4 reviewers, 1 supported the investigational indication, 2 supported the compassionate use of valves for treating prolonged air leaks, and the fourth thought that treatment of prolonged air leaks might be reasonable but had concerns about potential complications.

Practice Guidelines and Position Statements

In 2011, the British Thoracic Society published guidelines on advanced diagnostic and therapeutic flexible bronchoscopy in adults.[10] The guidelines stated that there is insufficient evidence to recommend the routine use of endobronchial valves for treatment of emphysema.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

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10. Du Rand IA, Barber PV, Goldring J, et al. Summary of the British Thoracic Society guidelines for advanced diagnostic and therapeutic flexible bronchoscopy in adults. Thorax. Nov 2011;66(11):1014-1015. PMID 22003155
11. Blue Cross Blue Shield Association. Medical Policy Reference Manual, No. 7.01.128 (June 2016).

Documentation for Clinical Review

Please provide the following documentation (if/when requested):

- History and physical and/or consultation notes including:
  - Reason for endobronchial valve use
  - Documentation of FDA HDE process and approval

Post Service

- Operative report(s)

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to benefit design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement.

IE

The following services may be considered investigational.

Type	Code	Description
CPT®	31647	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with balloon occlusion, when performed, assessment of air leak, airway sizing, and insertion of bronchial valve(s), initial lobe
	31648	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with removal of bronchial valve(s), initial lobe
	31649	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with removal of bronchial valve(s), each additional lobe (List separately in addition to code for primary procedure)
	31651	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with balloon occlusion, when performed, assessment of air leak, airway sizing, and insertion of bronchial

Type	Code	Description
		valve(s), each additional lobe (List separately in addition to code for primary procedure[s])
HCPCS	None	
ICD-10 Procedure	0BH38GZ	Insertion of Endobronchial Valve into Right Main Bronchus, Via Natural or Artificial Opening Endoscopic
	0BH48GZ	Insertion of Endobronchial Valve into Right Upper Lobe Bronchus, Via Natural or Artificial Opening Endoscopic
	0BH58GZ	Insertion of Endobronchial Valve into Right Middle Lobe Bronchus, Via Natural or Artificial Opening Endoscopic
	0BH68GZ	Insertion of Endobronchial Valve into Right Lower Lobe Bronchus, Via Natural or Artificial Opening Endoscopic
	0BH78GZ	Insertion of Endobronchial Valve into Left Main Bronchus, Via Natural or Artificial Opening Endoscopic
	0BH88GZ	Insertion of Endobronchial Valve into Left Upper Lobe Bronchus, Via Natural or Artificial Opening Endoscopic
	0BH98GZ	Insertion of Endobronchial Valve into Lingula Bronchus, Via Natural or Artificial Opening Endoscopic
	0BHB8GZ	Insertion of Endobronchial Valve into Left Lower Lobe Bronchus, Via Natural or Artificial Opening Endoscopic
ICD-10 Diagnosis	All Diagnoses	

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action	Reason
09/27/2013	BCBSA Medical Policy adoption	Medical Policy Committee
06/30/2015	Policy revision with position change	Medical Policy Committee
08/01/2016	Policy revision without position change	Medical Policy Committee

Definitions of Decision Determinations

Medically Necessary: A treatment, procedure, or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department. Please call (800) 541-6652 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.