Bronchial Valves

Policy # 00282
Original Effective Date: 12/15/2010
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Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers bronchial valves in all situations including, but not limited to the following to be **investigational:***

- Treatment of prolonged air leaks; and
- Treatment for patients with chronic obstructive pulmonary disease (COPD) or emphysema.

Background/Overview

AIR LEAKS
Proper lung functioning depends on the 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 from COPD.

Treatment
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 one-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; and
- Performing a thoracotomy with mechanical or chemical pleurodesis.

A bronchial valve is a device that permits one-way air movement. During inhalation, the valve is closed, preventing air flow into 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 bronchial 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.

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EMPHYSEMA
In emphysematous chronic obstructive pulmonary disease, 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.

Treatment
Use of bronchial valves in COPD is based on the improvement observed in patients who have undergone lung volume reduction surgery. Lung volume reduction surgery 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 the diseased lung. The procedure is designed to relieve dyspnea and improve functional lung capacity and quality of life; it is not curative. Bronchial valves have been investigated as a nonsurgical alternative to lung volume reduction surgery.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
In October 2008, the Spiration®‡ IBV System (Spiration, Redmond, WA) was approved by the U.S. FDA through 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 the normal inhalation phase of inspiration, or (3) present on normal expiration and accompanied by subcutaneous emphysema or respiratory compromise. Use of the intrabronchial Valve System is limited to 6 weeks per prolonged air leak. Use of the Spiration Intrabronchial Valve for emphysema is considered off-label. FDA product code: OAZ.

In December 2008, the Zephyr®‡ Endobronchial Valve (formerly by Emphasys Medical, now Pulmonx, Redwood City, CA) was considered by and FDA 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 May 2018, the Zephyr Endobronchial Valve has not been approved by FDA.

Centers for Medicare and Medicaid Services (CMS)
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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Rationale/Source

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

TREATMENT OF AIR LEAKS

Clinical Context and Therapy Purpose

The purpose of placing bronchial valves in patients who have pulmonary air leaks is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does placement of bronchial valves improve health outcomes in patients with pulmonary air leaks?

The following PICOTS were used to select literature to inform this review.

Patients

The relevant population of interest is individuals with pulmonary air leaks.

Interventions

The therapy being considered is the placement of bronchial valves.

Comparators

The following practice is currently being used: medical management.

Outcomes

The general outcomes of interest, in addition to overall survival, are a reduction in symptoms (eg, pneumothorax) and improvements in functional outcomes.

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Timing
Bronchial valves can be utilized for up to six weeks to effect resolution of a persistent pulmonary leak.

Setting
Placement of bronchial valves requires an inpatient surgical procedure.

Case Series
No RCTs or comparative observational studies were identified. Only case series and case reports are available.

In the largest case series, Travaline et al (2009) reported on 40 patients treated at 17 sites in the United States and Europe. The Zephyr Endobronchial Valve (EBV) was used. This device is not approved by the U.S. FDA. All patients in the series had prolonged pulmonary air leak (mean duration, 119 days; median, 20 days). The most common comorbidities were cancer and COPD. 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). Six patients experienced adverse events 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 was attributed to the valve or the implantation procedure.

Firlinger (2013) et al studied 13 patients with persistent, continuous air leak (ie, having an intrathoracic chest tube for >7 days despite conservative and/or surgical therapy) in Austria. Spiration valves were used in 9 patients and Zephyr valves in 4 patients. Ten (77%) of 13 patients were considered responders, defined as successful chest tube removal without need for further intervention. The Spiration IBV (intrabronchial valve) was used in six of ten responders and all three nonresponders.

Gillespie et al (2011) reported on a case series of 7 patients with pulmonary air leaks treated with Spiration IBV. The median duration of air leaks in the 7 patients before valve placement was 4 weeks (range, 2 weeks to 5 months). One patient had a second valve implanted due to an additional air leak. Complete air leak cessation occurred in 6 of 8 procedures after a mean duration of 5.2 days. The other 2 procedures resulted in a 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 from a patient who entered hospice care or the patient who underwent 2 procedures because the patient declined removal.

Section Summary: Treatment of Air Leaks
The only available data on bronchial valves for treating persistent air leaks are uncontrolled trials with small numbers of heterogeneous patients. Data on the FDA–approved Spiration IBV are particularly limited; Spiration valves were successfully placed in 7 patients in 1 case series and in 9 patients in another. This

evidence is inadequate to determine the impact of this technology on the net health outcome and does not it provide any comparative data with alternatives.

TREATMENT OF SEVERE OR ADVANCED EMPHYSEMA

Clinical Context and Therapy Purpose

The purpose of placing bronchial valves in patients who have severe or advanced emphysema is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does placement of bronchial valves improve health outcomes in patients with severe or advanced emphysema?

The following PICOTS were used to select literature to inform this review.

Patients

The relevant population of interest is individuals with severe/advanced emphysema.

Interventions

The therapy being considered is the placement of bronchial valves.

Comparators

The following practice is currently being used: medical management.

Outcomes

The general outcomes of interest, in addition to overall survival, are a reduction in symptoms and improvements in functional outcomes.

Timing

Improvement in lung function after use of bronchial valves as part of multimodality pulmonary care should be assessed at 6 months after insertion.

Setting

Placement of bronchial valves requires an inpatient surgical procedure.

Systematic Reviews

A Cochrane review by van Agteren et al (2017) included 5 trials with a total of 703 patients who were treated with the Zephyr EBV or medical management for COPD. Trials included were Endobronchial Valve for Emphysema Palliation Trial (VENT) (U.S. and E.U.), Bronchoscopic Lung Volume Reduction With Endobronchial Valves Reduces Dynamic Hyperinflation (BeLieVeR-HIFi) trial, IMPACT, and STELVIO. The VENT and BeLieVeR-HIFi trials are detailed below. The meta-analysis found that Zephyr valves led to significant improvements in lung function (including the forced air expiratory volume in 1 second [FEV_1]), quality of life (including St George's Respiratory Questionnaire [SGRQ]), and exercise capacity (6-minute

walk test [6MWT]; see Table 1). SGRQ scores range from 0 to 100, with higher scores indicating a worse quality of life. There were no significant differences in mortality rates between the 2 groups, but adverse events were more common in the EBV group.

The evidence on the Spiration IBV included 2 trials (Ninane et al [2012], IBV Valve Trial). One trial found a benefit for lung function (including FEV_1) and exercise capacity (6MWT) while the other did not. There were no significant differences in quality of life (including SGRQ scores) or mortality rates, but adverse events were more frequent in the IBV group.

Table 1. Results of Meta-Analysis

Outcomes	Zephyr EBV	95% CI	p	Spiration IBV	95% CI	p
FEV_1 SMD	0.48	0.32 to 0.64	<0.001	-2.15	-3.47 to -0.83	
SGRQ MD	-7.29 units	-11.2 to -3.45	<0.001	2.64	-0.28 to 5.56	*NS*
6MWT SMD	38.12	8.68 to 67.56	0.011	-19.54	-37.11 to -1.98	0.029
Mortality OR	1.07	0.47 to 2.43	*NS*	4.95	0.85 to 28.94	*NS*
Adverse events OR	5.85	2.16 to 15.84	<0.001	3.41	1.48 to 7.84	0.004

Adapted from van Agteren et al (2017).
CI: confidence interval; EBV: Endobronchial Valve; FEV_1: Forced air expiratory volume in 1 second; IBV: intrabronchial valve; MD: mean difference; OR: odds ratio; SGRQ: St. George's Respiratory Questionnaire; 6MWT: 6-minute walk test; SMD: standardized mean difference

Randomized Controlled Trials

Endobronchial Valve for Emphysema Palliation Trial

VENT was randomized but not blinded. Primary results were published by Sciurba et al (U.S. cohort) and Herth et al (European cohort). Key eligibility criteria for participation were diagnosis of heterogeneous emphysema, 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 post rehabilitation 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. Patients who remained eligible for the trial after undergoing the preliminary treatment program were randomized to therapy using the Zephyr EBV or to 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 6MWT distance. 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 by Valipour et al (2014). A limitation of the trial design was its lack of blinding, which could have influenced performance on the primary efficacy outcomes (eg, it might 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 (2010), 321 patients in the United States were randomized on a 2:1 basis to the Zephyr EBV (n=220) or standard medical care (n=101).[6] The mean number of valves placed in the Zephyr valve group was 3.8 per patient (range, 1-9 per patient). A total of 42 (19.1%) of 220 patients in the

Zephyr valve group and 28 (27.7%) of 101 in the control group had missing data for the primary efficacy outcomes. 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 2.

Table 2. Six-Month Primary Outcomes Data in the U.S. Cohort of VENT

Outcomes	EBV Group (n=220)	Control Group (n=101)	Between-Group Difference	p
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
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

Adapted from Sciurba et al (2010).
ABC: absolute percent change; CI: confidence interval; EBV: Endobronchial Valve; 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 SGRQ. At 6 months, the SGRQ score decreased by -2.8 points (95% confidence interval [CI], -4.7 to -1.0 points) in the EBV group and increased by 0.6 points (95% CI, -1.8 to 3.0 points) 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.[9] According to body plethysmography, the mean (standard deviation) change in total lung volume at 6 months was -1.2% (10.6%) in the EBV 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) but fell within the prespecified safety criteria. Adverse events to 6 months included 6 (2.8%) deaths in the EBV 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 EBV group followed had experienced COPD exacerbations; 22 of these events resulted in hospitalization. Over the same period, 8 (9.2%) of 87 patients in the control group had COPD exacerbations, all of which resulted in hospitalization. The difference in the 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 EBV group and none in the control group (p=0.02). Among the 214 patients who received valves and were followed for 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 (2012) reported on 171 patients in the European cohort of VENT; 111 patients were randomized to the EBV group and 60 patients to the standard care group. During the trial, 10 patients died and 4 patients withdrew. The number of patients 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 3 (outcomes reporting differed slightly from the U.S. cohort).

Table 3. Six-Month Primary Outcomes Data in the European Cohort of VENT

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
Mean (SD) change in cycle ergometry workload from baseline, W	2 (14)	-3 (10)	0.04

Adapted from Herth et al (2012).
ABC: absolute percent change.

At 12 months, mean (standard deviation) change in FEV_1 was 6 (26) in the EBV group and -2 (20) in the control group (p=0.05). The mean (standard deviation) change in cycle ergometry workload was 1 (13) watt in the EBV 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 et al (2012) 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 EBV group. There were 10 deaths, 6 in the EBV 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 EBV 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 scans at 6 months were reported by Valipour et al (2014). Of the 416 patients, 284 were in the EBV 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 measures in the Sciurba report. At 6 months, the mean target lobar volume reduction was significantly higher in patients

receiving EBV therapy (-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 BODE Index (a composite instrument that incorporates body mass index, an airflow obstruction metric, a dyspnea score, and exercise tolerance) at 6 months (p<0.001). (The index combines several variables, including the FEV_1 and 6MWT distance). A higher score on the index has been correlated with an increased risk of death from COPD. Valipour et al (2014) did not discuss missing data for the FEV_1 or 6MWT measures at 6 months.

Bronchoscopic Lung Volume Reduction With Endobronchial Valves Reduces Dynamic Hyperinflation Trial

A government-funded, BeLieVeR-HIFi trial evaluated the Zephyr EBV in a double-blind sham-controlled trial of 50 patients with heterogeneous emphysema and intact interlobar fissures. The patient population was based on the subgroup analysis of VENT, which showed greater efficacy of bronchial valves in patients with the following characteristics. Included were patients with an 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 in the COPD Assessment Test 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 bronchoscopy with sham valve placement. Valve placement led to statistically significant improvements in response rates for some outcomes compared with 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 COPD Assessment Test score (see Table 4). 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 4. Three-Month Response Rates for the BeLieVeR-HIFi Trial

Outcomes	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 time distance	52	17	0.012
Endurance cycle time	43	8	0.008
St. George's Respiratory Questionnaire score	48	46	1.0
COPD Assessment Test score	57	29	0.08

Adapted from Davey et al (2015).
COPD: chronic obstructive pulmonary disease.

The IBV Valve Trial

Wood et al (2014) reported on the IBV Valve Trial. Key eligibility criteria for participation in this randomized and double-blinded trial were age (40-74 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 trial participation, and patients eligible for lung volume reduction surgery or lung transplant received surgical counseling. All trial participants underwent anesthesia for bronchoscopy

and were then randomized on a 1:1 basis to active treatment (placement of IBV) or sham treatment (no valve placement). Patients were assessed at 1, 3, and 6 months. The primary effectiveness outcome was a composite measure including a change in the 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 a change in lobar lung volume measured by quantitative computed tomography. The computed tomography 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 the 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 patients. 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 5, 5% of patients in the treatment group and 0.7% in the control group were considered responders. Using 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 trialists found that the response rate in the treatment group was so low that it could not be considered a clinically meaningful finding.

Table 5. Composite Effectiveness Measure and Individual Components

Outcomes	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% to 9.212%[a]
St. George's Respiratory Questionnaire score			
No. of responders (≥ -4 points) (%)	39/121 (32.3%)	53/133 (39.8%)	-19.9% to 4.2%
Computed tomography volume, mL			
Mean upper-lobe change (SD)	-224 (299)	-17 (204)	-272 to -14[a]
Mean non-upper-lobe change (SD)	214 (384)	-27 (292)	155 to 326[a]

Adapted from Wood et al (2014).
BCrI: Bayesian credible interval.
[a] Statistically significant.

Regarding 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; no deaths were considered device-related. A pneumothorax occurred in 3 (2.1%) patients, all in the treatment group.

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Section Summary: Treatment of Severe or Advanced Emphysema
For patients with severe or advanced emphysema, 7 published RCTs and a systematic review of these trials have provided 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. For pooled trial data from the U.S. and European cohorts of VENT, 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 COPD Assessment Test score. Authors of the sham-controlled IBV Valve Trial concluded study findings did not indicate a clinically meaningful benefit of the Spiration IBV for patients with severe emphysema. Additionally, patients who received either bronchial valve device experienced numerous adverse events.

SUMMARY OF EVIDENCE
For individuals who have pulmonary air leaks who receive bronchial 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 bronchial valves for treating persistent air leaks derive from uncontrolled trials with small numbers of heterogeneous patients. Data on the Spiration IBV Valve System (approved by the U.S. FDA with a humanitarian device exemption) are particularly limited. While these valves were successfully placed in 40 patients in a multicenter case series and other series, these case series do not provide any comparative evidence with existing 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 bronchial valves, the evidence includes 7 RCTs and a systematic review of these trials. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, and treatment-related morbidity. Of the 7 randomized controlled trials, 5 did not use a FDA–approved valve. For the FDA–approved Spiration IBV Valve System, there was no improvement in the quality of life or exercise capacity in the combined results. Although some outcomes of the larger trials were statistically significant for bronchial valve treatment, the magnitude of the difference was generally of uncertain clinical significance. Moreover, the numerous adverse events experienced by patients who received bronchial 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.

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Policy History

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Current Effective Date: 11/21/2018

12/01/2010	Medical Policy Committee review
12/15/2010	Medical Policy Implementation Committee approval.
12/08/2011	Medical Policy Committee review
12/21/2011	Medical Policy Implementation Committee approval. No change to coverage.
12/06/2012	Medical Policy Committee review
12/19/2012	Medical Policy Implementation Committee approval. No change to coverage.
11/07/2013	Medical Policy Committee review
11/20/2013	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/06/2014	Medical Policy Committee review
11/21/2014	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
10/29/2015	Medical Policy Committee review
11/16/2015	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/03/2016	Medical Policy Committee review
11/16/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
11/02/2017	Medical Policy Committee review
11/15/2017	Medical Policy Implementation Committee approval. Title change. Coverage eligibility unchanged.
11/08/2018	Medical Policy Committee review
11/21/2018	Medical Policy Implementation Committee approval. No change to coverage.

Next Scheduled Review Date: 11/2019

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2017 by the American Medical Association (AMA).

Bronchial Valves

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CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	31647, 31648, 31649, 31651
HCPCS	No codes
ICD-10 Diagnosis	All related diagnoses

*****Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

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