Endobronchial 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 endobronchial valves in all situations including, but not limited to the following to be investigational:

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

Background/Overview

Proper lung functioning is dependent on a 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 a variety of processes including 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 COPD.

Although an air leak from the lung into the pleural space may seal spontaneously, it often requires intervention. Techniques currently employed to attempt air leak closure 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.

**FDA or Other Governmental Regulatory Approval**

**U.S. Food and Drug Administration (FDA)**

October 2008, the IBV™ Valve System (Spiration, Redmond, WA) was approved by the FDA through 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 (FEV1) 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 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.

**Rationale/Source**

**Treatment of Air Leaks**

No randomized controlled trials (RCTs) or comparative observational studies were identified. Only case series and case report data 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. Zephyr (Emphasys, now Pulmonx) 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 COPD. Prior to the procedure, 39 of the 40 patients had at least 1 chest tube. Five patients had other treatments, eg, blood patch before valve placement. The mean (SD) number of valves placed per patient was 2.9 (1.9) overall. After valve placement, 19 patients (47.5%) had complete resolution.
of acute air leak, 18 (45%) had a reduction in air leak, 2 (5%) had no change, and data were not available for 1 patient. The mean time from valve placement to chest tube removal was 21 days, and the median time was 7.5 days (data from 2 patients were 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 was highly variable, ranging from 5 to 1109 days. At last follow-up, 16 patients were reported to have died; none of the deaths were attributed to the valve or the valve implantation procedure.

The next largest case series published to date was 2013 study by Firlinger et al in Austria. The study included 16 patients with persistent continuous air leak, ie, having an intrathoracic chest tube for more than 7 days despite conservative and/or surgical therapy. Endobronchial valves were placed in 13 of 16 patients; the source of the air leak could not be identified in the other 3 individuals. U.S. FDA–approved Spiration IBV valves were used in 9 patients and Zephyr valves were used in the other 3 patients. Ten of 13 (77%) patients were considered responders, defined as successful chest tube removal without the 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. Target airways could not be identified in 2 patients, and valves were placed in 7 patients. One of the 7 had 2 procedures due to development of an additional air leak after the first one 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
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 evidence on comparisons 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 (VENT)

The VENT trial 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, FEV1 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 FEV1 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 (eg, it may have affected clinicians’ coaching of patients and/or the degree of effort exerted by patients).

U.S. 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). The mean number of valves placed in the endobronchial valve group was 3.8 per patient (range, 1-9). A total of 42 of 220 (19.1%) in the endobronchial valve group and 28 of 101 (27.7%) in the control group had missing data for the primary efficacy outcomes. Most of the 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 at 6 Months

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Endobronchial Valve Group (n=220)</th>
<th>Control Group (n=101)</th>
<th>Between-Group Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 mean absolute percent change from baseline (95% CI)</td>
<td>4.3% (1.4 to 7.2)</td>
<td>-2.5% (-5.4 to 0.4)</td>
<td>6.8% (2.1 to 11.5), p=0.005</td>
</tr>
<tr>
<td>Distance on 6-minute walk test median change from baseline (95% CI, m)</td>
<td>9.3 (-0.5 to 19.1)</td>
<td>-10.7 (-29.6 to 8.1)</td>
<td>19.1 (1.3 to 36.8), p=0.02</td>
</tr>
<tr>
<td>Median absolute percent change from baseline (95% CI)</td>
<td>2.5% (-1.1 to 6.1)</td>
<td>-3.2% (-8.9 to 2.4)</td>
<td>5.8% (0.5 to 11.2), p=0.04</td>
</tr>
</tbody>
</table>

CI: confidence interval; FEV1: forced 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 -2.8 points (95% confidence interval [CI], -
4.7 to -1.0) in the endobronchial valve group and increased 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 points generally considered to represent a clinically meaningful difference. 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) 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 or ventilator-dependent respiratory failure for >24 hours). The rate by 6 months was 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 different (p=0.08) and fell within the prespecified safety criteria. The adverse events to 6 months included 6 deaths (2.8%) in the endobronchial valve group and no deaths in the control group (p=0.19). Between 3 and 12 months, 25 of 214 (11.7%) patients in the endobronchial valve group followed over this time experienced COPD exacerbations; 22 of these events resulted in hospitalization. Over the same time period, 8 of 87 (9.2%) 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 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 cases (2.8%) of valve expectoration, aspiration, or migration and 9 cases (4.2%) 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 Findings**

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

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

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Endobronchial Valve Group (n=220)</th>
<th>Control Group (n=101)</th>
<th>P Value for Between-Group Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;</td>
<td>Mean (SD) absolute percent change from baseline</td>
<td>7% (20%)</td>
<td>0.5% (19%)</td>
</tr>
<tr>
<td>Distance on 6-minute walk test</td>
<td>Median (SD) change from baseline, m</td>
<td>15 (91)</td>
<td>10 (78)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD) change in cycle ergometry workload change from baseline, W</td>
<td>2 (14)</td>
<td>-3 (10)</td>
</tr>
</tbody>
</table>
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FEV₁: forced air expiratory volume in 1 second.

At 12 months, mean (SD) change in FEV₁ 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 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 reported that serious complications and the rate 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 longer 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 period, there were 13 cases of valve expectoration, aspiration or migration; this represented 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). 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. 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 FEV₁ 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 FEV₁ 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. 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 FEV₁ 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 FEV₁ (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 a 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

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

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

### IBV Valve Trial

The study, published by Wood et al in 2014, was randomized and double-blind. Key eligibility criteria for study 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 followed up 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 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 methods. 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, 144 to the treatment group and 135 to the control group. A total of 121 patients in the treatment group (85%) and 134 in the control group (99%) 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

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Treatment Group (n=142)</th>
<th>Control Group (n=135)</th>
<th>Difference (Treatment – Control), 95% BCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite measure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. or responders (%)</td>
<td>6/121 (5.0%)</td>
<td>1/134 (0.7%)</td>
<td>0.048%, 9.212%</td>
</tr>
<tr>
<td>SGRQ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of responders (≥ -4 points, %)</td>
<td>39/121 (32.3%)</td>
<td>53/133 (39.8%)</td>
<td>-19.9%, 4.2%</td>
</tr>
<tr>
<td>CT volume, mL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean UL change (SD)</td>
<td>-224 (299)</td>
<td>-17 (204)</td>
<td>-272, -14a</td>
</tr>
<tr>
<td>Mean NUL change (SD)</td>
<td>214 (384)</td>
<td>-27 (292)</td>
<td>155, 326a</td>
</tr>
</tbody>
</table>

BCI: Bayesian credible interval; NUL: non upper lobe; SGRQ: St. George’s Respiratory Questionnaire; UL: upper lobe.

a Statistically significant.

In terms of safety, there were significantly more patients with 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 patients (2.1%) in the treatment group and none in the control group.

Section Summary

For patients with advanced or severe emphysema, the 2 published RCTs provide insufficient evidence that the technology improves the net health outcome. The first trial, VENT, was limited by a lack of blinding and a large amount of missing data. Also, in VENT, findings on primary outcomes were mixed; there was a statistically significant change in FEV1 and in the 6-minute walk distance from baseline to 6 months in the U.S. cohort but not in the European cohort, and a statistically significant change in FEV1 at 12 months in the European cohort. In both trials, primary outcomes that were statistically significant were of magnitudes that represented uncertain clinical significance. Authors of the sham-controlled IBV Valve Trial concluded that their study findings did not indicate a clinically meaningful benefit of endobronchial valves for patients with severe emphysema. In addition, in both trials, patients who received endobronchial valves experienced numerous adverse events. In the IVB Valve Trial, the rate of serious adverse events was significantly higher in the treatment group than 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

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01812447a</td>
<td>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)</td>
<td>270</td>
<td>Sep 2016</td>
</tr>
<tr>
<td>NCT01989182a</td>
<td>The Spiration Valve System for the Treatment of Severe Emphysema (SVS)</td>
<td>100</td>
<td>Sep 2016</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Clinical Investigation</th>
<th>NCT #</th>
<th>Title</th>
<th>Number of Patients</th>
<th>Dates</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT02382614&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Safety and Effectiveness of the Spiration Valve System (SVS) in Air Leaks (VAST)</td>
<td>200</td>
<td>Dec 2016</td>
<td></td>
</tr>
<tr>
<td>NCT02022683&lt;sup&gt;a&lt;/sup&gt;</td>
<td>A Multi-center, Prospective, Randomized, Controlled Trial of Endobronchial Valve Therapy vs. Standard of Care in Heterogeneous Emphysema (TRANSFORM)</td>
<td>78</td>
<td>Feb 2018</td>
<td></td>
</tr>
<tr>
<td>NCT01796392&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Lung Function Improvement After Bronchoscopic Lung Volume Reduction With Pulmonx Endobronchial Valves Used in Treatment of Emphysema (LIBERATE)</td>
<td>183</td>
<td>Dec 2020</td>
<td></td>
</tr>
</tbody>
</table>

NCT: national clinical trial.
<sup>a</sup> Denotes industry-sponsored or cosponsored trial

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, input was received through 1 physician specialty society and 3 academic medical centers while this policy was under review for March 2011. Those providing input generally agreed that use of endobronchial valves is investigational for the treatment of 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.

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 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 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.
Endobronchial Valves

Policy # 00282
Original Effective Date: 12/15/2010
Current Effective Date: 11/16/2016

References

Policy History
Original Effective Date: 12/15/2010
Current Effective Date: 11/16/2016
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
11/06/2014 Medical Policy Committee review
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
01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes

Next Scheduled Review Date: 11/16/2017

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 2015 by the American Medical Association (AMA). 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.
Endobronchial Valves

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

<table>
<thead>
<tr>
<th>Code Type</th>
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<tbody>
<tr>
<td>CPT</td>
<td>31647, 31648, 31649, 31651</td>
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<tr>
<td>HCPCS</td>
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<tr>
<td>ICD-10 Diagnosis</td>
<td>All related diagnoses</td>
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*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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