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# Medical Policy

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| **Subject:** | Endobronchial Valve Devices | | |
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## Description/Scope

This document addresses the use of endobronchial valve devices (EBVs). This type of device is intended to provide one-way airflow blockage in segmental or subsegmental bronchi for individuals with pulmonary conditions complicated by air leaks or hyperinflation. Endobronchial valve devices are usually placed transorally into the lungs using flexible bronchoscopic tools.

**Note:** Please see the following documents for related information:

- CG-REHAB-03 Pulmonary Rehabilitation
- CG-SURG-110 Lung Volume Reduction Surgery

## Position Statement

**Medically Necessary:**

The use of endobronchial valve devices (EBV) is considered **medically necessary** for the treatment of individuals with severe emphysema when all of the following criteria are met:

A. Severe emphysema as demonstrated by all of the following:
   1. Forced expiratory volume (FEV1) is less than 45% predicted; **and**
   2. Total lung capacity (TLC) is greater than or equal to 100% predicted; **and**
   3. Residual volume (RV) is greater than or equal to 180% predicted;

**AND**

B. Pulmonary physiology suggests likely to benefit from EBV as demonstrated by:
    1. Targeted lobe shows little to no collateral ventilation (CV);

**AND**

C. Functional and health parameters suggest~~s~~ likely to benefit from EBV as demonstrated by all of the following:
    1. 6-minute walk distance greater than 140 meters*; **and**
    2. Nonsmoking for greater than 4 consecutive months; **and**
    3. Body mass index (BMI) greater than 15 kg/m$^2$ and less than 35 kg/m$^2$.

*-**Note**: For individuals who are unable to complete a six-minute walk due to mobility challenges unrelated to their pulmonary disease, please submit a letter of medical necessity documenting the reason the test could not be completed and indicate how functional reserve was determined to be adequate to benefit from the requested device.

**Not Medically Necessary:**

The use of endobronchial valve devices is considered **not medically necessary** when the above criteria are not met and for all other indications.

## Rationale

The use of endobronchial valves (EBVs) has been investigated for the treatment of various pulmonary conditions complicated by air leaks or hyperinflation. The available literature addresses two devices, the Zephyr® endobronchial valve (Pulmonx; Redwood City, CA), and the Spiration® Valve System ([SVS], Olympus; Redmond, WA), formerly known as IBV® Valve System.

*EBV for Emphysema*

Liu (2015) published the results of a meta-analysis including studies by Sciurba, Herth, and Ninane. The overall results indicated that EBV use yielded greater increase in forced expiratory volume ($FEV_1$%) than standard medications (weighted mean difference [WMD]: 6.71; p=0.0001), and resulted in a significant change in St. George's Respiratory Questionnaire (SGRQ) score (WMD: -3.64; p=0.002), modified Medical Research Council (mMRC) dyspnea score (WMD: -0.26; p=0.004), and cycle ergometry workload (WMD: 4.18; p<0.0001). They also reported that a similar level was evident for 6-minute walk

distance (6MWD) (WMD: 11.66; p=0.13). Alternatively, they stated that EBV use may increase the rate of hemoptysis (relative risk [RR], 5.15; p=0.03), but did not increase the adverse events including mortality, respiratory failure, empyema, pneumonia, or pneumothorax. The authors concluded that:

> EBV lung volume reduction for advanced emphysema showed superior efficacy and a good safety and tolerability compared with standard medications and sham EBV. More randomized controlled trial (RCT) studies are needed to pay more attention to the long-term efficacy and safety of bronchoscopic lung volume reduction with EBV in advanced emphysema.

Davey (2015) published the results of the BeLieVeR-HIFi study, a double-blind RCT which enrolled 50 individuals with heterogeneous emphysema and intact interlobar fissures who were assigned to treatment with either the Zephyr endobronchial valve (n=25) or a sham procedure (n=25). All subjects were followed for 3 months post-operatively. Significant improvements in the EBV group compared to the control group were noted with regard to increased $FEV_1$ (L) (median 0.06 L [0.02-0.38] versus 0.03 L [0-0.06]; p=0.0273), 6-minute walking time (6MWT) (25 meters vs. 3 meters; p=0.0119), and change in endurance time (25 seconds vs -10.8 seconds, p=0.0256). In the EBV group, 8 subjects were scored as having complete lung collapse in the isolated portion of the lung, 5 with a band of atelectasis, 2 with some volume reduction, and 8 with no change. There were 2 deaths in the EBV group and 1 control subject was unable to attend the follow-up assessment because of a prolonged pneumothorax. Additionally, 2 EBV subjects had pneumothorax responding to standard therapy, and 4 EBV subjects expectorated the valves before 3 months. These were replaced in 3 of the 4 subjects. The authors concluded that unilateral lobar occlusion with EBVs produced significant improvements in lung function, but there was a risk of significant complications.

Zoumot (2017) published an open-label, extension study of the BeLieVeR-HIFi trial that enrolled 12 subjects from the control group subsequently treated with EBVs and 19 from the experimental group without collateral ventilation (CV) who were followed for an additional 3 months. The authors reported that in CV negative subjects, FEV1 (L) increased by 0.19 L (0.25; mean [standard deviation SD]), residual volume (RV) was reduced by 0.49 L (0.76), the 6MWD increased by 32.6 m (68.7) and the SGRQ for COPD score improved by 8.2 points (20.2). Atelectasis or complete lobar collapse on CT was reported in 8 of 12 subjects treated with valves and another 2 had significant volume loss.

Klooster (2015) published the STELVIO trial, a blinded RCT involving 34 subjects with severe emphysema assigned to treatment with the Zephyr endobronchial valve compared to 34 subjects assigned to standard medical care. Subjects were followed for 6 months following EBV placement. The EBV group had 9 subjects lost to follow-

up vs. 1 subject in the control group. In the 6-month follow-up, the authors reported the EBV treatment group improved the $FEV_1$ by an average of 161 mL (80-242 mL) compared with the control group that improved by 21 mL (-9-52 mL). The forced vital capacity (FVC) showed an improvement of 416 mL (201-631 mL) in the EBV group compared with 69 mL (-50-187 mL) in the control group. The change in distance reported in the 6MWT for the EBV group improved an average of 60 m (35-85 m), and the control group declined by 14 m (-25 to -3 m). The authors reported that EBV-related "unacceptable adverse events" had occurred in 7 of 34 (21%) of EBV group subjects. Overall, 23 serious adverse events were noted in the EBV group vs. 5 in the control group ($p<0.001$), including pneumothorax ($p=0.02$) and additional events requiring valve removal or replacement procedures. Pneumothorax was reported in 6 of 34 EBV subjects (18%). Klooster (2017) published 1-year follow-up results for 40 of the original 64 subjects (62.5%, both the original treatment group and control group subjects that crossed over to treatment) involved in the STELVIO trial. They reported that significant improvements (defined as $p<0.001$) were found for $FEV_1$, RV, 6MWD, and SGRQ. The authors indicated for STELVIO the clinical important differences for $FEV_1$ as a 10% increase, a 430 ml reduction in RV, a 26-m increase for the 6MWT, and a 4-point reduction in the SGRQ. A total of 2 subjects died; 1 after 58 days due to progressive respiratory failure and 1 after 338 days of follow-up due to a myocardial infarction. Valve replacement was done in 17% of subjects and 22% had permanent valve removal. Pneumothoraces occurred in 22% of subjects before 6 months, and none occurred between 6 and 12 months.

Trudzinski (2016) published findings from their retrospective analysis of 20 subjects with severe emphysema that were treated with EBV. All subjects were required to be compliant with maximum medical therapy and completed smoking cessation at least 3 months prior to valve placement. Inclusion criteria required subjects to have $FEV_1 \leq$ 20% predicted, diffusing capacity for carbon monoxide (DLCO) < 20% predicted, and the target lobe for treatment was determined by assessing CV. After treatment, atelectasis occurred in 11 of the 19 subjects (55%). The mean clinically important difference (MCID) for $FEV_1$ (increase of > 100mL) was achieved in 5/20 cases, with a mean difference of improvement of 0.11 L (± 0.15 L; $p=0.001$). MCID for RV (decrease of > 430mL) was reached in 11/19 cases, with a mean difference of –1.10 L (± 1.64 L; $p=0.005$). The 6MWT also met MCID (increase of > 26 m) with a mean difference of +50 m (± 0.51 m; $p=0.191$). Pneumothorax occurred in 5 subjects (25%), all within 24 hours of intervention. Valve removal was necessary in 2 subjects due to persistent air leaks. There were no cases of pneumonia, valve migration, or loss of valves reported.

Valipour (2016), reported the results of the IMPACT study, a multicenter RCT of EBV plus standard of care (SoC) or SoC alone in subjects with severe homogeneous emphysema and no CV. A total of 93 subjects were enrolled with 43 receiving EBV treatment with Zephyr endobronchial valves and 50 randomized to SoC alone. The primary outcome measured the percentage change in $FEV_1$ at 3 months post procedure compared to baseline and showed

there was an improvement of 13.7 ± 28.2% (mean ± SD) in the group that received EBV. The SoC group showed a decline in $FEV_1$ by 3.2 ± 13%, therefore the mean difference between the groups is 17.0% (95% confidence interval [CI], 8.1-25.8%; p=0.0002). Secondary outcome results between the groups showed a difference of 9.6 points for SGRQ (p<0.0001), 40 m for 6MWD (p=0.002), and 480 ml for RV (p=0.011) with results favoring the EBV treatment group. The 3-month follow-up visit included reporting of adverse events; there were reports of 12 pneumothoraces that occurred in 11 subjects (25.6%), with the majority occurring on the day of the procedure. Valves were replaced in 3 subjects, and 1 subject required removal and replacement of 2 valves due to migration. There was 1 death reported in the 3-month follow-up period; the subject was randomized to the SoC group and suffered from a pulmonary infection. Additional studies are needed to determine optimal placement of valve(s) to achieve maximum benefit with improvements in $FEV_1$.

Lee (2017) published a case series study involving 21 subjects with emphysema who had undergone bronchoscopic lung volume reduction surgery (LVRS) with an unspecified valve device reported improvement in ventilation-perfusion mismatch. The authors reported significant improvement in $FEV_1$ (p<0.001) and 6-minute walking distance (p=0.002). Additionally, both ventilation per voxel (a basic volume building block of 3-D images), (p<0.001), and total ventilation (p=0.01) improved. However, neither perfusion per voxel (p=0.16) nor total perfusion (p=0.49) changed significantly. They did note that subjects who had undergone lung volume reduction of 50% or greater had significantly better improvement in $FEV_1$ (p=0.02) and ventilation per voxel (p=0.03) compared to those receiving less than 50% reduction. Finally, the ventilation/perfusion ratio (V/Q mismatch) also improved (p=0.005), mainly owing to the improvement in ventilation though the imaging technique used to measure V/Q mismatch has few studies confirming this imaging technique for this purpose in subjects with COPD. ~~Therefore~~Therefore, the CT imaging chosen to verify the primary endpoint also requires further study to ensure the validity of the data.

A meta-analysis by Kumar (2017) involved four trials encompassing 159 subjects who had received EBV treatment. They reported that the pooled mean difference at 6 months for $FEV_1$ was 0.146 L (p<0.001), 6MWT was 45.225 meters (p<0.001), and SGRQ was -8.825 points (p=0.004). All the pooled mean differences were statistically significant and higher than their respective minimal clinically important difference. Adverse events that were associated with EBVs included pneumothorax, valve migration, pneumonia, and COPD exacerbation. The authors conclude that additional investigation is needed to further clarify the optimal population to receive treatment with EBVs as the data shows promise of improvement though it must be carefully considered due to the risk of adverse events.

Kemp (2017) published the results of the prospective, multicenter TRANSFORM study, which involved 97 subjects with severe heterogeneous emphysema assigned in a 2:1 fashion to treatment with either EBVs plus SoC (n=65) or SoC alone (n=32). At 3 months postoperative, $FEV_1$ improvement ≥ 12% was reported in 55.4% of the EBV group subjects and 6.5% of control subjects (p<0.001). These improvements were maintained to the 6-month follow-up point (56.3% vs. 3.2%, respectively; p<0.001). The mean % change in $FEV_1$ at 6 months was reported to be 20.7 ± 29.6% in the treatment group and -8.6 ± 13.0% in SoC. Target lobe volume reduction (TLVR) ≥ 350 ml was reported in 89.9% of EBV subjects (mean 1.09 ± 0.62 L, p<0.001). Between-group differences for changes at 6 months were statistically and clinically significant, with the ΔEBV-SoC for RV=700 ml; 6-minute walk distance (6MWD) +78.7 m; SGRQ -6.5 points; Modified Medical Research Council (mMRC) Dyspnea score -0.6 points; and BODE Index -1.8 points (p<0.05 for all). Pneumothorax was the most common adverse event, occurring in 19/65 (29.2%) of EBV subjects.

Fiorelli (2017) described the results of a retrospective case series study including 33 subjects with heterogeneous emphysema treated with the Zephyr device followed for a minimum of 5 years. Of the original 33 subjects, 3 underwent sequential contralateral valve placement. Subjects were stratified into those with post-treatment lobar collapse (n=27) and those without (n=9). The mean number of valves used was 2.3. Overall, improvement was reported within the collapse group for $FEV_1$%, baseline was 34 ± 6.8% versus 5-year 50 ± 5.5% (p=0.001); FVC% result at baseline was reported as 32 ± 4.5% versus 5-year 48 ± 2.7% (p=0.002); RV% at baseline was 247 ± 37% and measured 207 ± 8.3% at 5 years (p=0.003); 6MWT was 189 ± 54 m at baseline and improved to 280 ± 33 m at 5 years (p=0.001); and SGQR score at baseline was 61 ± 3.8 compared with 44 ± 2.9 at the 5 year follow-up (p=0.001). These results were retained for the entire follow-up without significant decline, as confirmed by Bonferroni post-hoc analysis. The no-collapse group had no significant benefits for these measures. The 1-, 2-, 3-, 4- and 5-year survival rates were 100%, 90%, 78%, 71% and 71%, respectively. The collapse group had a better survival than the no-collapse group (45 vs. 24 months; p=0.001). No major complications or deaths were reported. Removal of valves was required in 3 subjects due to hemoptysis, bronchospasm, and migration. A single subject expectorated one valve, which was replaced.

Low (2018) published the results of a meta-analysis that evaluated the evidence from five RCTs including 703 subjects who received EBVs for emphysema. The authors reported that percentage change of $FEV_1$ in EBV subjects was significantly improved vs. controls (WMD =11.43%; p<0.0001). Similar benefits were reported in the SGQR score (WMD=−5.69; p=0.0002). No differences were demonstrated in the 6-minute walking test (WMD=14.12; p=0.14). The complication rate after EBV was significantly increased for pneumothorax (RR, 8.16; p=0.002), any hemoptysis (RR, 5.01; p=0.04)] and valve migration (RR, 8.64; p=0.004). The authors concluded that treatment

with EBV results in short-term improvement in lung function and quality of life. However, there is an increased risk of minor hemoptysis, pneumothorax, and valve migration.

Criner (2018) reported the results of the LIBERATE trial, a RCT involving 190 subjects randomized in a 2:1 fashion to treatment with EBV (n=128) or SoC (n=62). Subjects were between 40 and 70 years of age with heterogeneous emphysema, post-bronchodilator $FEV_1$ 15-45% predicted, total lung capacity (TLC) > 100% predicted, RV ≥ 175% predicted, DLCO ≥ 20% predicted, BMI <35 $kg/m^2$ and a 6MWD of 100-500 m after supervised pulmonary rehabilitation. The report included follow-up through 12 months, with plans for an additional 4 years of follow-up. At baseline, mMRC Dyspnea score and Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage classification were imbalanced between groups (p=0.091 and p=0.037, respectively); however, neither of these imbalances impacted the primary or secondary outcomes. A median of 4 valves were implanted per subject with a total of 501 placed. The majority were placed in the left upper lobe (66.4%). Only 11 EBV group subjects underwent post-placement valve adjustment procedures at 45 days. A total of 28 procedures were needed for valve removal or replacement following adverse events (including 12 pneumothoraces, 2 increased dyspnea, 1 respiratory failure, 1 hypoxia, 1 subcutaneous emphysema, and 1 valve migration). Complete removal of all valves was conducted in 8 subjects prior to the end of the 12-month study period; 2 valves were expectorated and 3 migrated during that same period. The primary endpoint, an increase ≥ 15% over baseline in post bronchodilator $FEV_1$, was reported in 47.7% of EBV group subjects and 16.8% of control subjects (p<0.001 in the intent-to-treat population). Similarly, the secondary endpoints, between-group differences with regard to absolute change in $FEV_1$, SGRQ scores, and 6MWD were all significantly in favor of the EBV group (p<0.001, p=0.0004, and p=0.002, respectively). TLVR was significantly improved at both 45 days and 12 months in the EBV group (p=0.001 for both), with 79.1% and 74.2% of subjects reaching minimal clinical difference (MCID) at 45 days and 12 months. Likewise, reduction in hyperinflation as measured by RV and TRV/TLC ratio was reported (p<0.001 for both). RV decrease of 310 ml or more was reported in 61.6% of the EBV group and 22.4% of controls at 12 months. Improvement in gas exchange and mMRC dyspnea score were both significantly better in the EBV group as well (p=0.013 and p<0.01, respectively). No significant differences were noted when an analysis of valve location was conducted (upper vs. lower lobes). Significantly more EBV group subjects experienced serious respiratory adverse events vs. control subjects in the first 45 days (35.2% vs. 4.8%, p<0.001); this included death (4 vs. 0), pneumothorax (34 vs. 0), COPD exacerbation (10 vs. 3), respiratory failure (2 vs. 0), and pneumonia (1 vs. 0), respectively. The 4 deaths reported in the EBV group had 3 that were considered "definitely" related to the EBVs and the last "probably" related. During the longer term, out to 12 months, the overall frequency of events was not significantly different (33.6% vs. 30.6%, p=not significant [NS]), but the rate of pneumothoraces continued to be higher in the EBV group (44 vs. 0, p<0.001). An additional death in the EBV group was reported, but was not deemed related to the treatment. There were no outcomes differences between the EBV groups with (n=44) vs.

without (n=84) pneumothoraces. The authors reported that subjects with "complex" pneumothorax (defined by either death or removal of all EBVs) vs. "simple" pneumothorax (all other pneumothoraces) were at higher risk of developing a "complex" pneumothorax if the lobe with maximum destruction score was not treated, and the non-treated contralateral lung destruction score was greater than 60%. The authors concluded that treatment with the Zephyr EBV in individuals with severe emphysema selected for little to no CV between the treated and the ipsilateral lobe resulted in significant lobar volume reduction, reduction in hyperinflation, and clinically meaningful improvements in dyspnea, lung function, exercise capacity, and quality of life. Though benefits are associated with successful placement of valves, this study demonstrated that individuals treated with EBVs experience a significantly higher rate of pneumothorax in the short term (27% in the EBV group vs. 0% in the control group). The analysis indicated that proper selection of subjects and placement of valves could avoid such complications.

Li (2019) reported the results of the REACH RCT involving 99 subjects with emphysema. Inclusion criteria included mMRC ≤ 2, post-bronchodilator $FEV_1$ ≤ 45%, total lung capacity ≥ 100%, RV ≥ 150%, highly diseased target lobe (≥ 40% emphysema involvement), high heterogeneity compared to the ipsilateral lobe (≥ 15% difference), and an intact interlobar fissure (≥ 90% complete). Subjects were assigned to treatment with either the SVS (n=66) or SoC (n=33). No significant differences between groups were noted at baseline with regard to primary and secondary outcome measures ($FEV_1$, total lung capacity or volume, SGRQ, Chronic Obstructive Pulmonary Disease Assessment Test [CAT], mMRC scales, and 6MWT) or emphysema involvement, heterogeneity score, or fissure integrity. Mean $FEV_1$ improvements from baseline to 3 months were 0.104 L in the EBV group vs. 0.003 L in the control group (p=0.001). The authors noted that this satisfied the primary effectiveness endpoint. Using a threshold of ≥ 15% improvement in $FEV_1$ from baseline, the treatment group responder rate was 49, 48, and 41% compared to 22, 13, and 21% in the control group at 1, 3, and 6 months, respectively. Statistically significant mean reductions of 684 mL and 757 mL at 3 and 6 months were reported in the EBV group. The authors noted that using a TLVR threshold of 350 mL, 52.5% and 66.1% of treatment subjects were responders at the 3- and 6-month time points. Results from the 6MWT and SGRQ indicated mean improvements in the treatment group through all of the time points. However, significant differences between groups were~~as~~ reported for only the 6-month follow-up, when the control group showed a marked deterioration. Statistically significant differences between groups were~~as~~ only shown for the CAT at the 6-month follow-up as the mean score decreased by 2.17 in the treatment group and increased by 1.94 in the control group (p=0.017). No differences between groups with regard to mMRC were~~as~~ reported. The relative percent improvement in 6MWT between the two groups was 3.0, 8.4, and 15.5% over the 1-, 3-, and 6-month follow-ups, respectively, but was statistically significantly different only at 6 months. The SGRQ results showed a similar trend over time, with relative differences between the groups of 10.9, 7.2, and 10.5 points at 1, 3, and 6 months, respectively (p=0.005 at 1-month and p=0.007 at 6 months). Valve replacement or revision procedures occurred in 12 subjects, with an

additional 29 valves placed, and 4 removed. Subjects with repeat valve procedures had a TLVR at 3 and 6 months on average 200 mL less than that obtained by the entire treatment population. An overall serious adverse event rate of 33% was reported for the EBV group and 24.2% for the control group. Acute exacerbations of COPD were reported in 7 subjects and device and procedure-related pneumothoraces in 5 subjects. No deaths were reported in the treatment group, whereas 1 occurred in the control group. No valve migrations or expectorations were reported. The authors noted that use of MCID of 350 mL reduction was used, but recent studies indicate that a greater TLVR is necessary to achieve MCID. The authors concluded that treatment with the SVS for individuals with severe heterogeneous emphysema offers benefit, the observed complications and need for repeat procedures raises significant concerns as to whether the SVS device materially improves the net health outcome for this population.

Criner (2019) reported on the EMPROVE open-label, RCT. Subjects with heterogeneous emphysema with severe dyspnea, a 6MWD of ≥ 140 m, free from cigarette smoking for a minimum of 4 months, $FEV_1 \leq 45\%$ predicted, RV ≥ 150% predicted, TLC ≥ 100% predicted, and a BMI ≥ 15 kg/m$^2$ were randomized to SVS with SoC (n=113) or SoC alone (n=59). Follow-up assessments were conducted for 2 years in the control group and up to 5 years in the treatment group. The primary efficacy endpoint was the mean change in $FEV_1$ between treatment and control groups at 6 months. At 6 months, the treatment group reported an improved $FEV_1$ of 0.099 L from baseline, and the control group reported -0.002 L from baseline, resulting in a group difference of 0.101 L (95% Bayesian credible interval [BCI], 0.060-0.141). The 6-month outcome measure responder rate for $FEV_1 \geq 15\%$ for the treatment group was 39/106 (36.8%) of subjects, and 12 months was 32/86 (37.2%). The 12-month results show an improvement of 0.067 L in the treatment group and the control group showed a decrease of 0.032 L, with a between-group difference of 0.099 L (95% BCI, 0.048-0.151). The secondary outcomes showed improvement in the treatment group including a mean residual volume/target lobe volume (RV/TLV) of -0.039 (95% BCI, -0.058 to -0.020; 1.0000, posterior probability [PP]) at 6 months. The responder rate for outcome measures within the treatment group at 6 months for TLV ≥ 350 mL reduction was 76/102 (74.5%). There was only a slight mean improvement in the treatment group for the SGRQ at 6 months, with a between-group difference of 213.0 points (95% BCI, 217.4 to 28.5; 1.0000, PP), with the responder rate for SGRQ ≥ 4 point reduction occurring in 57/105 (54.3%) of subjects. The 6MWT was not statistically different between the groups at 6 months. Serious adverse events (SAE) within the first 6 months occurred in 31.0% of the treatment group and 11.9% of the SoC group. The treatment group primarily had increased incidence of pneumothorax; 32 events were reported with 18 classified as 'serious' (in 16 of 113 treatment subjects) and 14 reported as non-serious (in 13 of 113 treatment subjects). SAEs between 6 and 12 months included 21.4% in the treatment group versus 10.6% in the SoC group, and 3 other SAEs reported that were device related including 1 death. There was a total of 4 deaths in the treatment group, and 3 deaths in the SoC group.

Gompelmann and colleagues (2019a) published findings of survival after EBV in subjects with severe emphysema. A total of 449 subjects met inclusion criteria and were treated with SVS (n=93), Zephyr valves (n=282), or both (n=74). Subjects completed imaging after valve placement and were stratified into one of two subgroups, those that achieved complete atelectasis, or partial or no atelectasis achieved. The atelectasis group consisted of 29.2% (128/439, 10 subjects were lost to follow-up); of the 128 individuals, 34 had a pneumothorax. The non-atelectasis group had a total of 70.8% (311/439), with pneumothorax found in 50 subjects. Valve removal was required in 32.1% (144/449) of the subjects as a result of no benefit or lost benefit. Throughout the study a total of 152 subjects died. The subjects that achieved lobar atelectasis showed survival benefit compared with subjects without atelectasis. The 4-year survival rate was 77.1% (atelectasis) versus 59.4% (non-atelectasis), and 5-year survival rate was 65.3% compared to 43.9% (p=0.019, after adjusting for age). A pneumothorax event did not influence survival as the 4-year survival rate was 67% for the pneumothorax group versus 62.8% for non-pneumothorax group.

Gompelmann and colleagues (2019b) published an analysis on the long-term follow up for individuals with severe emphysema after EBV. This analysis followed 256 individuals with severe emphysema, significantly reduced $FEV_1$, severe hyperinflation, and absent CV. Atelectasis occurred in 31.5% (79/251, 5 subjects did not complete follow-up imaging), 46.2% (116/251) resulted in incomplete atelectasis or no volume change and did not have a pneumothorax, 8.4% (21/251) had both atelectasis and pneumothorax, and 13.9% (35/251) had only pneumothorax. The 3-year follow-up consisted of 66 individuals, 114 were lost to follow-up, 49 individuals died, and 27 had additional treatment. Of the 66 that completed the 3-year follow-up, 20 individuals achieved complete lobar atelectasis, and 25 had partial or no atelectasis. Pneumothorax occurred in 21 of the 66 subjects, and 10 of those had achieved atelectasis. A total of 24.6% (63/256) of individuals required permanent removal of the valves due to lack of benefit, pneumothorax, definitive LVRS, pneumonia, lung cancer, respiratory insufficiency, or pulmonary infections.

Dransfield (2020) published a post-hoc analysis of the LIBERATE trial, specifically the dyspnea, activity levels, and quality of life measures. The self-administered questionnaires were not previously published. The unblinded questionnaires were completed at baseline and follow-up visits, though the individuals were not reminded of their baseline scores at follow-up visits. The mean group difference (Zephyr Group-SOC) of the Transitional Dyspnea Index (TDI), focal score was 4.3 points from baseline to 12-month follow-up (p<0.001). The Borg after 6MWT difference was -0.9 points (p<0.001); the Exacerbations of Chronic Pulmonary Disease Tool (EXACT)-PRO, dyspnea domain had a difference of -8.8 points (p=0.002); and the CAT scored -0.6 points for the mean difference (p=0.002). There were more responders within the treatment group for the TDI, focal score that had a greater than or equal to 1-point increase in their score compared with the SoC group, 61.9% versus 15.8%, respectively (p<0.001). There was no statistically significant improvement in the responders for the Borg dyspnea score after the

6MWT over the SoC group. The TDI, magnitude of task results showed a greater than or equal to 1-point increase in 60.5% of treatment group compared with 13.8% of the SOC group (p<0.001). The TDI, magnitude of effort also showed greater response of greater than or equal to 1-point increase within the treatment group when compared to SOC with 58.3% versus 15.5%, respectively (p<0.001). The TDI, functional improvement results were similar with 57.9% of treatment group scoring greater than or equal to 1-point increase and 15.5% of SOC (p<0.001). The treatment group self-reported daily diary scores had a higher number of days at 206 days when symptom intensity was improved from baseline compared with SOC that had 102 days (p<0.001), the treatment group also reported fewer days that were worse than baseline at 95 days compared with 122 days reported by SOC (p<0.001). These results expand on the previously reported measures from the LIBERATE trial and though the tools used may be subject to recall bias, the results do correlate with the clinical benefits associated with reduction in hyperinflation.

van Dijk (2020) published the results of a retrospective single-center study evaluating EBV treatment from 2016-2018 for individuals with emphysema and DLCO ≤ 20% predicted. A total of 20 individuals were included and were considered responders to treatment if the relative change in $FEV_1$ was ≥ 12%, the RV decreased ≥ 430 mL, the 6MWD increased by ≥ 26 m, and SGRQ scores decreased by 4 or 7 points. The 6-month follow-up results showed an improvement in all lung function parameters, the 6MWD, and the SGRQ score. The responder rates at 6 months for $FEV_1$ was 45%, RV was 40%, SGRQ -4 points was 65%, SGRQ -7 points was 50%, and the 6MWD was 45%. There was no statistical difference in lung parameters, 6MWD, SGRQ total score, and responder rate between the DLCO ≤20% group and the control group which consisted of individuals with DLCO >20% predicted. Pneumothorax requiring chest tube occurred in 3 individuals, with 1 requiring removal of the device and 3 others had pneumothorax that did not require treatment. Other adverse events included 3 individuals experiencing a hospital admission due to COPD exacerbation, 3 individuals required additional bronchoscopies for valve replacement and 1 individual required removal due to migration which resulted in loss of atelectasis due to extensive granulation tissue.

In 2019, Pulmonx began enrollment for a multi-center, single-arm, registry study to assess the safety and effectiveness of the Zephyr device. The goal of this observational study is to enroll approximately 150 subjects to be followed for 3 years. The primary outcomes of the trial will be serious adverse events, including pneumothorax, and measures of pulmonary function (Pulmonx Corporation, 2020).

Low (2022) reported the results of a study involving data from the U.S. Food and Drug Administration's (FDA) Manufacturers and User Device Experience (MAUDE) database on adverse events related to use of the Zephyr EBV. Data from May 2019 to June 2020 was included. A total of 124 adverse events were included in the report. Pneumothorax was the most-reported adverse event, representing 89% (110/124) of total adverse events. Among

subjects with pneumothorax, 54 (49%) had resolution with initial pleural catheter placement. The remaining subjects developed persistent air leaks, despite initial pleural catheter placement, requiring further intervention. Of the subjects with persistent air leaks, 28 subjects (52%) had their EBVs removed, 12 (22%) had Heimlich valve placed and were discharged with the pleural catheters, and 10 (19%) underwent additional pleural catheter placement. A total of 14 deaths were reported, with 12 occurring during the same inpatient stay following EBV placement. Of these 12, 11 had persistent pneumothorax. An additional 2 deaths occurred following readmission. Other adverse events reported included acute hypoxic respiratory failure (n=6, 5%), pneumonia (n=4, 3%), hemoptysis (n=2, 1.6%), valve migration (n=1, 1%), and pleural effusion (n=1, 1%). The results of this study are limited by the nature of the MAUDE database, including reporting bias, incomplete reporting, and other issues. The authors concluded that further studies are needed to estimate the true magnitude of the complications associated with EBV placement.

Posthuma (2022) reported a study involving the real-life use of EBVs in a retrospective single center cohort study. The authors reported that out of a sample of 350 subjects who were potential candidates for EBV placement, a total of 55 (16%) underwent the procedure and 45 (12.8%) had complete 3-month follow-up data. Of the 10 subjects not included in the final group of 45, 6 subjects had their valves removed due to severe pneumothorax (n=2) or lacking treatment benefit (n=4). After 1-year follow-up, 34 of the 45 (76%) treated subjects had their EBV intact. The authors reported that the most common reason for removal of EBV was loss of benefit, mostly due to granulation tissue (n=5). One subject died, but it was determined that it was not related to treatment with EBVs. At 1 year the mean change in FEV1 was +101 ± 176 mL ($p<0.05$), RV −527 ± 842 mL ($p<0.05$), and 6MWD +7 ± 55 m ($p>0.05$). The most common adverse events were airway infections requiring antibiotics and post-intervention COPD exacerbations. At least 1 complication was experienced by 54.5% of subjects, most of which were easily manageable and not considered severe. The pneumothorax rate was 9%, and all cases were treated with a pleural chest catheter. Single or complete valve removal was performed in 6 subjects. The authors concluded that with only 16% of screened subjects being eligible for EBV placement, it appears that this intervention is likely only applicable in a small subset of highly selected subjects with advanced emphysema.

In 2022 Hartman and colleagues reported the results of a retrospective cohort study involving 1471 subjects with severe COPD, including emphysema. Of these, 483 subjects were treated with either EBVs (n=353) or endobronchial coils (n=130). In the intervention group, 165 subjects (34%) died during follow-up. The median survival time was significantly longer in the endobronchial intervention group vs. the non-endobronchial intervention group (3133 days vs. 2503 days, $p<0.001$). No significant difference in median survival time was noted between subjects treated with coils vs. EBVs (3171 days versus 3133 days). Multiple other factors significantly negatively influenced survival, including male gender, higher age, higher number of packyears, higher

number of hospitalizations for a COPD exacerbation, and others. Not undergoing the endobronchial treatment was an independent predictor of mortality (Hazard Ratio [HR], 2.016, p<0.001). This data cannot be used to evaluate the use of EBVs alone, as the report did not provide adequately stratified data for that purpose.

Recent meta-analysis reports included 18 different trials pooled across ~~3~~ several studies, and each concluded that EBV improved lung function as demonstrated by $FEV_1$ measurements, 6MWT, and SGRQ, compared with SoC. The three meta-analysis reports included individuals with moderate to severe emphysema; Labarca (2019) and Majid (2020) reviewed EBV alone and had comparable inclusion criteria. ~~The~~ A third study compared the various options for bronchoscopic lung volume reduction (BLVR) and therefore required a different set of inclusion criteria (Xu, 2020). Candidates for EBV must be carefully considered and should have severe emphysema and hyperinflation, with the absence of CV for best possible outcomes. Patel (2022) reported significant improvement in $FEV_1$, percentage $FEV_1$%, SGRQ, 6MWD, and RV in the EBV group compared with SoC. The risk of pneumothorax was consistently reported to be higher in individuals that receive EBV treatment versus SoC across all three meta-analysis reports.

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) released the updated Global strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease in 2021, which provides recommendations for the use of bronchoscopic interventions. The recommendation for EBV was upgraded to an A in the 2020 edition, this recommendation, in part, is based on the aforementioned EMPROVE trial (Criner, 2019). The GOLD recommendation states the following:

> In select patients with advanced emphysema, bronchoscopic interventions reduce end-expiratory lung volume and improve exercise tolerance, health status and lung function at 6-12 months following treatment.
> Endobronchial valves (Evidence A), Lung coils (Evidence B), vapor ablation (Evidence B)

It should be noted that a rating of Evidence A is defined by GOLD as follows:

> Randomized controlled trials (RCT): Evidence is from endpoints of well-designed RCTs that provide consistent findings in the population for which the recommendation is made without any important limitations.
> Rich body of high quality evidence without any significant limitation or bias: Requires high quality evidence from greater than 2 clinical trials involving a substantial number of subjects, or a single high quality RCT involving substantial numbers of patient without any bias.

While some uncertainty persists as to the likelihood of any given individual benefiting from EBV placement, there are relevant specialty society recommendations supporting this treatment method based on ~~the~~ literature ~~is~~ concordant in showing some benefit which outweighs associated risks when used in carefully selected patients with severe emphysema who have significant hyperinflation with air trapping, ~~and~~ pulmonary physiology suggests likely to benefit from EBV, including little to no evidence of collateral ventilation, and ~~,~~functional and health parameters suggests likely to benefit from EBV. This last factor has traditionally been demonstrated by candidates not smoking in the previous 4 months, having a moderate Body Mass Index (BMI) and can perform adequately in the 6-MWD test. In some instances, individuals with mobility limitations may not be able to perform a 6-MWD test, but are still reasonable candidates toe treatment with EBVs. In such cases the treating provider should use alternative methods of assessing the individual's functional capacity when available. ~~In addition, use in this population is supported by relevant specialty society guidelines.~~

*EBV for Pulmonary Air Leaks*

EBVs have also been proposed for the treatment of pulmonary air leaks. The vast majority of the available literature addressing this approach has been in the form of case reports (Anile, 2006; ~~Dalar~~Dakar, 2013; De Giacomo, 2006; Feller-Kopman, 2006; Ferguson, 2006; Mitchell, 2006; Schweigert, 2010; Snell, 2005; Yu, 2019). However, there are case series studies that have been reported. The largest available case series study published to date was conducted by Travaline and others (2009), and reported on the outcomes of 40 subjects with prolonged pulmonary air leaks treated with the Zephyr device. At the end of a mean 66 days of follow-up (range 7-166 days), 47.5% of subjects had complete resolution, 45.0% had a significant reduction, and 5.0% had no change in condition. In total, 6 of the 40 subjects had adverse reactions due to valve placement including valve expectoration, oxygen desaturation, valve malpositioning requiring replacement, and pneumonia. At the end of the study period, 8 of the subjects had the valves removed.

Firlinger (2013) reported on 13 consecutive subjects with high comorbidity and evidence of continuous air leaks and chest tubes for at least 7 days. A total of 9 subjects received SVS, and 4 received Zephyr valves. Ten subjects were considered responders (6 subjects received SVS, 4 received Zephyr), and 3 were non-responders (all received SVS). After valve implantation, air leak flow decreased significantly from 871 ± 551 mL/min to 61 ± 72 mL/min immediately after the intervention ($p<0.001$). The mean duration of chest tube drainage was 18 ± 8 days before and 9 ± 6 days after the intervention ($p<0.01$). Long-term follow-up was available for 9 subjects. No adverse events related to the valve implantation were reported. Seven subjects underwent valve removal without any further complications.

Dooms and colleagues (2014) described the use of EBVs in 10 subjects who had undergone lung cancer resection surgery with subsequent persistent air leaks refractory to conservative therapy. The median air leak cessation was reported to be 2 days after treatment. Overall, a significant decrease in $FEV_1$ was found at airway closure by valve implantation (p=0.0002). Chest tube removal occurred at a median of 4 days (range 1-14 days). A total of 3 subjects experienced a recurrence of limited air leaks (< 50% of initial value) due to valve displacement without migration. Upon bronchoscopic evaluation, shallow depth of the bronchus was reported as the cause. No deaths, no cardiovascular complications, and no implant-related events were reported. Ultimately, 1 subject suffered from respiratory insufficiency requiring negative positive pressure ventilation for 2 weeks until the valves were removed.

In 2018, Yu and colleagues described a retrospective case series study involving 37 subjects with persistent (at least 1 week) air leaks complicating spontaneous pneumothorax in which surgical intervention was not feasible. The Zephyr device was implanted in 19 subjects and the remaining 18 subjects underwent SoC. The mean number of valves used in the EBV group was 3.6. The authors reported successful treatment in 8 of 19 subjects. However, 1 subject had recurrence within 2 hours of treatment. Of the remaining 7, chest tube removal occurred within 2 days. In the remaining 11 subjects with EBV treatment failure, 3 subjects had immediate success with failure soon afterwards and persisting beyond 72 hours. The other 8 subjects had temporary air leak reduction which persisted beyond 72 hours. There was a statistically significant difference between the EBV and no-EBV groups with regard to the number of days from first bronchoscopy to air-leak cessation, according to the Gehan-Breslow-Wilcoxon test (p=0.027), but not the log-rank test (p=0.138). EBV use was significantly associated with air leak cessation (adjusted ~~Hazard Ratio [~~HR~~]~~, 2.39). No incidences of valve displacement were reported. All subjects in the no-EBV group survived, whereas 3 subjects in the EBV group died within 30 days of endobronchial valve implantation. In 2 of these subjects, death was deemed not related to the EBV, and in the third the relationship was uncertain. The surviving 16 subjects had their valves removed at a median of 43 days.

Huang (2018) describes the use of the Zephyr device in 11 subjects with persistent postoperative air leaks (n=6) or secondary spontaneous pneumothorax (n=5) who had evidence of continuous air leak flow with whose chest tubes remained in place for more than 7 days. The authors reported that the number of valves used varied from 1 to 3 (median=1), with significant heterogeneity in anatomic placement. Complete resolution of air leaks was reported in 8 subjects (72.7%), including all 5 with spontaneous pneumothorax. For this latter group, the mean duration of air leak before and after valve deployment was 19.4 and 6 days, respectively. In the post-op group, 3 subjects were considered responders, and 1 expectorated the valve 1 day following placement and underwent subsequent operative treatment. The remaining 2 had some improvement with EBV placement, but also underwent subsequent

operative treatment. The mean duration of air leak before and after valve deployment in this group was 58.5 and 4.5 days, respectively. There were no complications related to the valve deployment reported.

Flora and colleagues (2020) published the results of a retrospective review for SVS use in persistent air leaks (PAL) secondary to pulmonary infections. A total of 19 individuals underwent 23 procedures and average time from first chest tube placement to SVS placement was 23.4 ± 20.8 days. Chest tubes were successfully removed in 19/22 (86.4%) of the alveolar-pleural fistula (APF) events with no additional intervention required. The average time from procedure to chest tube removal was 20.1 ± 24.8 days and when corrected for 6 of the APF events that required prolonged chest tubes due to evacuation of pleural fluid, the corrected average time is 12.8 ± 20.2 days. A total of 9 adverse events occurred within the first 30 days of implant, 3 individuals passed away (2 withdrawal of care and 1 had a ruptured vessel due to lung necrosis), 2 PALs required talc pleurodesis, 1 migration required revision, 1 individual with mechanical-ventilator associated pneumonia developed contralateral PAL, 1 chest tube dislodgement, and 1 ingestion of foreign object during intubation. Further studies comparing both types of valve systems and a standard control group are needed for PALs due to infectious etiologies as the valve size could play a role in management. SVS has a larger surface area allowing drainage of secretions and clarification of benefit as well as assessing risk is needed, as current literature lacks comparison.

The limited evidence available regarding EBVs for pulmonary air leaks have significant methodological limitations, further study is warranted.

## Background/Overview

In individuals with severe emphysema, diseased tissues progressively lose their elasticity and fail to expand and contract properly leading to hyperinflation that impedes air flow and gas exchange. Emphysema is often heterogeneous, occurring more severely in certain areas.

One method of treating heterogeneous emphysema is LVRS. This procedure has been developed to remove the most diseased lung tissue, providing more space in the chest cavity for healthier lung tissue to expand, and resulting in improved ventilation and lung function. LVRS is a surgical procedure and it has only been used in the most serious cases.

Some individuals may develop air leaks in lung tissue due to a wide variety of reasons, including trauma, disease or due to complications of surgery. An air leak in the pulmonary tract may be due to a hole between the lung and the

pleural space, or a passageway that has been created between functional lung tissue and adjacent tissues. Air leaks significantly impair lung function and usually require surgical treatment if they do not spontaneously resolve.

EBV devices have been developed as a method to isolate diseased portions of the lung as an alternative to LVRS. These devices are deployed into segmental or subsegmental bronchi and allow the flow of air and secretions out of the targeted portion of the lung but prevent return flow. The devices may be permanently implanted or can be removed at a later date, if needed. Prevention of return air flow causes a reduction in the size of diseased portions of the lung, allowing expansion of healthier tissue and reducing hyperinflation.

The Spiration Valve System (SVS), was granted a humanitarian device exemption (HDE) in March 2006 by the FDA for the indication of 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 (~~LVRS~~)~~. SVS was granted Premarket approval (PMA) by the FDA in 2018 for adults with shortness of breath and hyperinflation associated with severe emphysema in regions of the lung that have evidence of low CV. The SVS device consists of an endobronchial valve and a deployment catheter. Using a flexible bronchoscope, the catheter is used to place the small umbrella-shaped valve into the lung. The Pulmonx Zephyr Endobronchial Valve was granted PMA by the FDA in June 2018 for the bronchoscopic treatment of adults with hyperinflation associated with severe emphysema in regions of the lung that have little to no CV.

## Coding

*The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. 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.*

**When services may be medically necessary when criteria are met:**

| **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 |
| 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 |

**ICD-10 Procedure**

| | |
|---|---|
| 0BH30GZ-0BH38GZ | Insertion of endobronchial valve into right main bronchus [by approach; includes codes 0BH30GZ, 0BH33GZ, 0BH34GZ, 0BH37GZ, 0BH38GZ] |
| 0BH40GZ-0BH48GZ | Insertion of endobronchial valve into right upper lobe bronchus [by approach; includes codes 0BH40GZ, 0BH43GZ, 0BH44GZ, 0BH47GZ, 0BH48GZ] |
| 0BH50GZ-0BH58GZ | Insertion of endobronchial valve into right middle lobe bronchus [by approach; includes codes 0BH50GZ, 0BH53GZ, 0BH54GZ, 0BH57GZ, 0BH58GZ] |
| 0BH60GZ-0BH68GZ | Insertion of endobronchial valve into right lower lobe bronchus [by approach; includes codes 0BH60GZ, 0BH63GZ, 0BH64GZ, 0BH67GZ, 0BH68GZ] |
| 0BH70GZ-0BH78GZ | Insertion of endobronchial valve into left main bronchus [by approach; includes codes 0BH70GZ, 0BH73GZ, 0BH74GZ, 0BH77GZ, 0BH78GZ] |
| 0BH80GZ-0BH88GZ | Insertion of endobronchial valve into left upper lobe bronchus [by approach; includes codes 0BH80GZ, 0BH83GZ, 0BH84GZ, 0BH87GZ, 0BH88GZ] |
| 0BH90GZ-0BH98GZ | Insertion of endobronchial valve into lingula bronchus [by approach; includes codes 0BH90GZ, 0BH93GZ, 0BH94GZ, 0BH97GZ, 0BH98GZ] |
| 0BHB0GZ-0BHB8GZ | Insertion of endobronchial valve into left lower lobe bronchus [by approach; includes codes 0BHB0GZ, 0BHB3GZ, 0BHB4GZ, 0BHB7GZ, 0BHB8GZ] |

**ICD-10 Diagnosis**

| | |
|---|---|
| J43.0-J43.9 | Emphysema |

**When services are Not Medically Necessary:**
For the procedure codes listed above when criteria are not met and for all other diagnoses not listed.

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**Government Agency, Medical Society, and Other Authoritative Publications:**

1. ClinicalTrials.gov. Pulmonx Corporation. Pulmonx endobronchial valves used in treatment of emphysema (LIBERATE study). NLM Identifier: NCT01796392. Last updated on July 10, 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT01796392. Accessed on August 4, 2022.
2. ClinicalTrials.gov. Pulmonx Corporation. Zephyr valve registry. NLM Identifier: NCT04186546. Last updated on April 29, 2021. Available at: https://clinicaltrials.gov/ct2/show/NCT04186546. Accessed on August 4, 2022.
3. ClinicalTrials.gov. Spiration, Inc. Evaluation of the Spiration® Valve System for emphysema to improve lung function (EMPROVE). NLM Identifier: NCT01812447. Last updated on April 18, 2019. Available at: https://clinicaltrials.gov/ct2/show/NCT01812447. Accessed on August 4, 2022.
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**The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.**

## Document History

| Status | Date | Action |
|---|---|---|
| Revised | 08/11/2022 | Medical Policy & Technology Assessment Committee (MPTAC) review. Updated hierarchy formatting in Position Statement. Added Note addressing individuals unable to perform a 6-Minute Walk Distance test. -Updated Rationale, References and Index sections. |
| Revised | 08/12/2021 | ~~Medical Policy & Technology Assessment Committee (~~MPTAC~~)~~ review. Added MN indications, revised Investigational NMN statements to NMN. Updated Coding, Description/Scope, Rationale, Background/Overview, and References sections. |
| Reviewed | 08/13/2020 | MPTAC review. Updated Rationale, Background/Overview and References sections. |
| Reviewed | 08/22/2019 | MPTAC review. Updated Rationale and References sections. |
| Reviewed | 09/13/2018 | MPTAC review. Updated Rationale and References sections. |
| Reviewed | 02/27/2018 | MPTAC review. The document header wording updated from "Current Effective Date" to "Publish Date." Updated Rationale and References sections. |
| Reviewed | 02/02/2017 | MPTAC review. Updated Rationale and References sections. |
| Reviewed | 02/04/2016 | MPTAC review. Updated Rationale and Reference sections. Removed ICD-9 codes from Coding section. |
| Reviewed | 02/05/2015 | MPTAC review. |
| Reviewed | 02/13/2014 | MPTAC review. Updated Rationale and Reference sections. |
| Reviewed | 02/14/2013 | MPTAC review. Updated Rationale and Reference sections. |
| | 01/01/2013 | Updated Coding section with 01/01/2013 CPT changes; removed 0250T, 0251T, 0252T deleted 12/31/2012. |
| Reviewed | 02/16/2012 | MPTAC review. |
| Reviewed | 02/17/2011 | MPTAC review. Updated Rationale and Reference sections. |
| New | 11/18/2010 | MPTAC review. Initial document development. |





This Medical Policy provides assistance in understanding Healthy Blue's standard Medicaid benefit plan. When evaluating coverage for a specific member benefit, reference to federal and state law, as well as contractual requirements may be necessary, since these may differ from our standard benefit plan. In the event of a conflict with standard plan benefits, federal, state and/or contractual requirements will govern. Before using this policy, please check all federal, state and/or contractual requirements applicable to the specific benefit plan coverage. Healthy Blue reserves the right to modify its Policies and Guidelines as necessary and in accordance with legal and contractual requirements. This Medical Policy is provided for informational purposes. It does not constitute medical advice. Healthy Blue may also use tools and criteria developed by third parties, to assist us in administering health benefits. Healthy Blue's Policies and Guidelines are intended to be used in accordance with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.