Bronchial thermoplasty for the treatment of asthma is considered investigational.

The following category I CPT codes are specific for this procedure:
- **31660** Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with bronchial thermoplasty, 1 lobe
- **31661** Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with bronchial thermoplasty, 2 or more lobes

Bronchial thermoplasty is a potential treatment option for patients with severe persistent asthma. It consists of radiofrequency energy delivered to the distal airways with the aim of decreasing smooth muscle mass believed to be associated with airway inflammation.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

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

In April 2010, the Alair® Bronchial Thermoplasty System (Asthmatx, Sunnyvale, CA, now part of Boston Scientific) was approved by the U.S. Food and Drug Administration (FDA) through the premarket approval process for use in adults with severe and persistent asthma whose symptoms are not adequately controlled with low-dose inhaled corticosteroids and long-acting β-agonists. Use of the treatment is contraindicated in patients with implantable devices and those with sensitivities to lidocaine, atropine, or benzodiazepines. It should also not be used while patients are experiencing an asthma exacerbation, active respiratory infection, bleeding disorder, or within 2 weeks of making changes in their corticosteroid regimen. The same area of the lung should not be treated more than once with bronchial thermoplasty. FDA product code: OOY.
Rationale

Background

Asthma

Asthma, a chronic lung disease, affects approximately 7.6% of adults and 8.4% of children in the United States and, in 2014, accounted for approximately 440,000 hospitalizations and 3650 deaths. Asthma symptoms include episodic shortness of breath that is generally associated with other symptoms such as wheezing, coughing, and chest tightness. Objective clinical features include bronchial hyperresponsiveness, airway inflammation, and reversible airflow obstruction (at least 12% improvement in forced expiratory volume in 1 second postbronchodilator, with a minimum of 200 mL improvement). However, there is substantial heterogeneity in the inflammatory features of patients diagnosed with asthma, and this biologic diversity is responsible, at least in part, for the variable response to treatment in the asthma population.

Management

Management of asthma consists of environmental control, patient education, management of comorbidities, and regular follow-up for affected patients, as well as a stepped approach to medication treatment. Guidelines from the National Heart, Lung and Blood Institute has defined 6 pharmacologic steps: step 1 for intermittent asthma and steps 2 through 6 for persistent asthma. The preferred daily medications: step 1: short-acting \( \beta \)-agonists as needed; step 2: low-dose inhaled corticosteroids (ICS); step 3: ICS and long-acting \( \beta \)-agonists (LABA) or medium-dose ICS; step 4: medium-dose ICS and LABA; step 5: high-dose ICS and LABA; and step 6: high-dose ICS and LABA, and oral corticosteroids.

Despite this multidimensional approach, many patients continue to experience considerable morbidity. In addition to ongoing efforts to implement optimally standard approaches to asthma treatment, new therapies are being developed. One recently developed therapy is bronchial thermoplasty, the controlled delivery of radiofrequency energy to heat tissues in the distal airways. Bronchial thermoplasty is based on the premise that patients with asthma have an increased amount of smooth muscle in the airway and that contraction of this smooth muscle is a major cause of airway constriction. The thermal energy delivered via bronchial thermoplasty aims to reduce the amount of smooth muscle and thereby decrease muscle-mediated bronchoconstriction with the ultimate goal of reducing asthma-related morbidity. Bronchial thermoplasty is intended as a supplemental treatment for patients with severe persistent asthma (i.e., steps 5 and 6 in the stepwise approach to care).

Bronchial thermoplasty procedures are performed on an outpatient basis, and each session lasts approximately 1 hour. During the procedure, a standard flexible bronchoscope is placed through the patient’s mouth or nose into the most distal targeted airway and a catheter is inserted into the working channel of the bronchoscope. After placement, the electrode array in the top of the catheter is expanded, and radiofrequency energy is delivered from a proprietary controller and used to heat tissue to 65°C over a 5-mm area. The positioning of the catheter and application of thermal energy is repeated several times in contiguous areas along the accessible length of the airway. At the end of the treatment session, the catheter and bronchoscope are removed. A course of treatment consists of 3 separate procedures in different regions of the lung scheduled about 3 weeks apart.

Literature Review

Assessment of efficacy for therapeutic interventions involves a determination of whether the intervention improves health outcomes. The optimal study design for a therapeutic intervention is a randomized controlled trial (RCT) that includes clinically relevant measures of health outcomes. For conditions such as asthma, where there are subjective outcomes such as self-reported symptoms and frequency of as-needed medication, placebo- or sham-controlled randomized trials are needed to demonstrate that the intervention has a benefit beyond the placebo effect.
Bronchial Thermoplasty for the Treatment of Asthma
Randomized Controlled Trials

There are 3 industry-sponsored RCTs evaluating the efficacy and safety of bronchial thermoplasty; individual trials are described next.

Research in Severe Asthma Trial

This small Research in Severe Asthma (RISA) trial, published by Pavord et al in 2007, was conducted at 8 centers in the U.K., Brazil, and Canada. Eligibility criteria included age 18 or older; asthma diagnosis; uncontrolled symptoms, despite treatment with high-dose inhaled corticosteroids (ICSs; at least 750 μg fluticasone propionate per day or equivalent) and long-acting β-agonists (LABAs; at least 100 μg salmeterol per day or equivalent), with or without other medications including oral prednisone or leukotriene modifiers; forced expiratory volume in 1 second (FEV1) at least 50% of predicted; demonstrated airway hyperresponsiveness by challenge with methacholine or reversible bronchoconstriction during the prior 12 months; abstinence from smoking for at least 1 year, and a smoking history of less than 10 pack-years. After a 2-week run-in period, 34 participants were randomized to a control group (n=17) that received continued medical management alone or to medical management plus treatment with the Alair Bronchial Thermoplasty System (n=17). The bronchial thermoplasty group received 3 procedures at least 3 weeks apart (weeks 0-6). During weeks 6 to 22, all participants remained on a stable dose of steroids, and then, during weeks 22 to 36, an attempt was made to reduce the dose of oral corticosteroids (or ICSs for patients not taking the oral medication). Between weeks 36 and 52, patients took the reduced dose of steroids. A total of 32 (94%) of the 34 participants completed the study.

The primary outcomes of the trial were the rate of adverse events and serious adverse events (defined as any event that was fatal, required prolonged hospitalization, caused substantial immediate risk of death, resulted in permanent impairment, or required intervention to prevent permanent impairment). In the initial treatment period, 4 patients in the bronchial thermoplasty group experienced 7 serious adverse events requiring hospitalization; none occurred in the control group. During the remainder of the trial, 3 patients in the bronchial thermoplasty group experienced 5 serious adverse events, and 1 patient in the control group experienced 4 serious adverse events; all events required hospitalization. There were no significant differences between groups in other efficacy variables including morning and evening peak expiratory flow, symptom scores, number of symptom-free days, improvement in FEV1 predicted, and several quality-of-life (QOL) measures. The small sample size resulted in limited power to detect differences in the efficacy outcomes.

In 2013, Pavord et al published 5-year safety data on 14 (82%) of the 17 patients randomized to bronchial thermoplasty in the RISA trial. All 14 patients completed the 3-year evaluation, and 12 patients completed evaluations at 4 and 5 years. As previously described, safety outcomes were the primary outcomes of RISA. In year 1, each asthma symptom was considered an adverse event and, in subsequent years, multiple asthma symptoms were considered to be a single adverse event. Among those with follow-up data available, the number of patients with asthma adverse events in years 2, 3, 4, and 5 were 5 (36%), 7 (50%), 2 (17%), and 5 (42%), respectively. In addition, during years 2 to 5, there were 11 respiratory-related hospitalizations in 5 patients. The number of patients with data available was too small to draw reliable conclusions about long-term safety, and there were no long-term data available on patients in the control group.
Asthma Intervention Research Trial

Cox et al published findings of the Asthma Intervention Research (AIR) trial in 2007, which was designed to evaluate symptom control and adverse events following bronchial thermoplasty. Patients were recruited from the same 3 countries as the RISA trial plus Denmark. The eligibility criteria included age 18 to 65 years with moderate-to-severe persistent asthma requiring daily therapy with ICSs (equivalent to at least 200 μg beclomethasone) and LABAs (at least 100 μg salmeterol or equivalent). Also required for study entry were an FEV1 of 60% to 85% of predicted, airway hyperresponsiveness, stable asthma in the 6 weeks before enrollment, no current respiratory infection, and not more than 2 lower respiratory infections requiring treatment in the past year. An additional criterion was worsening asthma control during a 2-week baseline test period during which time LABAs were withheld. A total of 112 patients met eligibility following the baseline test phase and were randomized to medical management with ICSs and LABAs (n=56) or to the same medical management strategy plus bronchial thermoplasty (3 sessions approximately 3 weeks apart) (n=56). After follow-up visits at 3, 6, and 12 months, there was a 2-week period of abstinence from LABAs, during which data on exacerbations were collected. Between data collection periods, patients could use all maintenance therapies.

The primary outcome was the difference between groups in change in rate of mild exacerbations from the baseline 2-week abstinence period. An exacerbation was defined as the occurrence on 2 consecutive days of a reduction in the morning peak expiratory flow of at least 20% below the average value (recorded during the week before the abstinence period), the need for more than 3 additional puffs of rescue medication compared with the week before the abstinence period, or nocturnal awakening caused by asthma symptoms. The trial was powered to detect a difference between groups of 8 mild exacerbations per person per year. Data were available at 3 months for 100 (89%) of 112 patients and at 12 months for 101 (90%) patients; all patients were included in the safety analysis.

The mean (SD) number of mild exacerbations per person per week in the bronchial thermoplasty group was 0.35 (0.32) during the baseline test period and 0.18 (0.31) per person per week at 12 months (a decrease of 0.17 per person per week). In the control group, the mean (SD) number of mild exacerbations per person per week was 0.28 (0.31) at baseline and 0.31 (0.46) at 12 months (an increase of 0.03 per person per week). Compared with the control group, the bronchial thermoplasty group had a significantly greater reduction in mild exacerbations at the 12-month follow-up (p=0.003). Overall, the average number of exacerbations during the 2-week data collection periods at 3, 6, and 12 months decreased in the bronchial thermoplasty group by a mean (SD) of 0.16 (0.37) per person per week, but not in the control group, which had a mean increase of 0.04 (0.29) mild exacerbations. This resulted in a mean difference of 20 mild exacerbations per week or about 10 per year. In contrast, there was no significant difference between the numbers of severe exacerbations at any time point compared with baseline, but the trial may not have had sufficient statistical power for this outcome. At the 12-month follow-up, the mean (SD) number of severe exacerbations in the bronchial thermoplasty group was 0.01 (0.08) per person per week compared with 0.07 (0.18) at baseline. By contrast, the mean (SD) number of severe exacerbations in the control group was 0.06 (0.24) per person per week compared with 0.09 (0.31) at baseline.

The rate of adverse events was higher in the bronchial thermoplasty group during the active treatment period, but the proportion of adverse events was similar in the 2 groups in the posttreatment period. Posttreatment, 3 patients in the bronchial thermoplasty group required hospitalization and 2 patients in the control group required a total of 3 hospitalizations. A limitation of the trial is the lack of a sham intervention and, consequently, an inability to blind patients to treatment group.

In 2011, Thomson et al published 5-year data from the AIR trial. All trial participants who completed the 1-year follow-up visit were invited to participate in the extension study; 45 (87%) of 52 in the bronchial thermoplasty group and 24 (49%) of 49 in the control group opted to participate. Follow-up was done on an annual basis. Patients in the control group were followed...
for 2 additional years, and patients in the bronchial thermoplasty group were followed for 5 years. Twenty-one (88%) of 24 patients in the control group and 42 (93%) of 45 in the bronchial thermoplasty group completed the final follow-up. No instances of pneumothorax, intubation, mechanical ventilation, cardiac arrhythmias, or death were reported during the extension study. As previously stated, data were collected on both treatment groups during the first 2 years of the extension study. In the first year (year 2 of the study), the rate of hospitalizations was 3 (7%) of 45 in the bronchial thermoplasty group and 0 in the control group (p = 0.55). In year 3, the rate of hospitalizations in the bronchial thermoplasty group was again 3 (7%) of 45, and 1 (5%) of 21 patients in the control group (p = 1.00). Rates of emergency department visits in year 2 were 3 (7%) and 3 (12.5%) in the bronchial thermoplasty and control groups, respectively (p = 0.41); in year 3, rates were 3 (5%) and 3 (5%), respectively (p = 1.00). There was 1 hospitalization each of years 4 and 5 in the bronchial thermoplasty group.

In the extension study of the AIR trial, unlike the initial follow-up period, respiratory adverse events with multiple symptoms were recorded as a single adverse event. This could give a misleading impression of the total number of adverse events or relative number in the 2 groups. The incidence of respiratory adverse events during year 2 was 24 (53%) of 45 in the bronchial thermoplasty group and 13 (54%) of 24 in the control group. During year 3, incidence was 24 (56%) of 43 in the bronchial thermoplasty group and 12 (57%) of 21 in the control group; differences between groups were not statistically significant in year 2 or 3. The incidence of respiratory adverse events in the bronchial thermoplasty group was similar in subsequent years; rates were 23 (53%) of 43 in year 4 and 22 (52%) of 42 in year 5.

The Thomson study also reported 2 measures of lung function: postbronchodilator FEV₁ and forced vital capacity. Exact numbers were not reported, but postbronchodilator FEV₁ did not go below 80% of predicted in either group during years 2 to 5. The group comparisons of safety and efficacy in this follow-up trial were limited by the differential rate of follow-up between the 2 groups, with a lower percentage of patients in the control group agreeing to participate in the follow-up study.

**Asthma Intervention Research 2 Trial**

AIR2 was an RCT evaluating the efficacy of bronchial thermoplasty at 30 sites in 6 countries (including the United States); findings were published in 2010 by Castro et al. Unlike the other 2 RCTs, the control condition was a sham intervention, and the trial was double-blind. Eligibility criteria were similar to those in the AIR trial; key differences were that a higher initial dose of ICSs was required (equivalent to at least 1000 μg beclomethasone), and patients were required to have experienced at least 2 days of asthma symptoms during the 4-week baseline period and have a baseline score on the Asthma Quality of Life Questionnaire (AQLQ) of no more than 6.25. (The possible range of the AQLQ score is 1 to 7, with a higher number representing a better QOL.) Also different from the AIR trial, patients were not required to experience symptom worsening during a period of abstinence from LABAs. Patients were stable on their asthma medication and continued their regimens during the study. The primary outcome was the difference between groups in the change from baseline in the AQLQ score, with scores from the 6-, 9-, and 12-month follow-ups averaged (integrated AQLQ score). A related outcome was the proportion of patients who achieved a change in their AQLQ score of 0.5 or greater, generally considered the minimally important difference for this scale. Bayesian analysis was used. The target posterior probability of superiority (PPS) of bronchial thermoplasty over sham was 95% except for the primary AQLQ end point; there the target was 96.4% to adjust for 2 interim looks at the data. The prior for the analysis was not reported in the article.

A total of 297 patients were randomized, 196 to a bronchial thermoplasty group and 101 to a sham control group. The intervention for all participants consisted of 3 bronchoscopy procedures, performed 3 weeks apart. Participants and outcome assessment was blinded, but the intervention team was unblinded. The sham intervention was identical to the active treatment, except that no radiofrequency energy was delivered. Nine participants withdrew consent before beginning treatment, and 288 underwent bronchoscopy and were included in
the intention-to-treat (ITT) population. One hundred eighty-five participants in the treatment group and 97 in the sham control group underwent the second bronchoscopy, and the same numbers of patients had the third bronchoscopy (it is not clear whether they were exactly the same patients). A total of 278 (94%) of the 297 enrolled patients completed the 12-month visit, 181 in the treatment group and 97 in the sham control group.

The superiority of bronchial thermoplasty was not achieved in the ITT population for the primary effectiveness outcome, mean change in the integrated AQLQ score. Mean (SD) change was 1.35 (1.10) in the bronchial thermoplasty group and 1.16 (1.23) in the sham control group. Using Bayesian analysis, the PPS was 96%. This did not surpass the target PPS of 96.4%. However, superiority of bronchial thermoplasty on a related outcome was achieved. In the ITT population, the percentage of patients achieving an AQLQ score change of 0.5 or greater (i.e., at least the minimally important difference) was 79% in the bronchial thermoplasty group and 64% in the control group. The PPS at 99.6% surpassed the target probability for secondary outcomes of 95%. Additional analysis of data from the active treatment group suggested that responders (defined as a change in AQLQ score of at least 0.5) were more likely to have a lower baseline score than nonresponders (mean, 4.1 vs 5.1, respectively).

Several secondary outcomes favored bronchial thermoplasty over the sham control group. They include a reduction in the proportion of patients reporting asthma worsening during follow-up (27.3% vs 42.9%, respectively; PPS=99.7%) and a reduction in the number of emergency department visits (0.07 vs 0.43 visits per person per year, respectively; PPS=99.9%). Moreover, there was a reduction in severe exacerbations of 0.47 per person per year in the bronchial thermoplasty group compared with 0.70 per person per year in the control group (PPS=95.5%). There were no significant differences between groups in other secondary efficacy outcomes, including morning peak expiratory flow, number of symptom-free days, symptom score, and rescue medication use.

For safety outcomes, during the treatment phase, there was a higher rate of respiratory adverse events in the active treatment group (85% of participants; mean, 1.0 events per bronchoscopy) compared with the sham group (76% of participants; mean, 0.7 events per bronchoscopy). A total of 16 (8.4%) patients in the active treatment group required 19 hospitalizations for respiratory symptoms during the treatment phase compared with 2 (2%) patients in the sham group, who required 1 hospitalization each. However, during the posttreatment period, 70% of patients in the bronchial thermoplasty group and 80% of patients in the sham group reported adverse respiratory events. During this phase of the trial, 5 (2.6%) patients in the bronchial thermoplasty group had a total of 6 hospitalizations for respiratory symptoms, and 4 (4.1%) patients in the sham group had 12 hospitalizations (1 patient had 9 hospitalizations).

In the AIR2 trial, the sham group had a relatively high rate of response (e.g., 64% experienced a clinically significant increase in the AQLQ score). Blinding appeared to be initially successful and remained so for the sham group. Participants in both groups were unable to correctly guess their treatment group after the first bronchoscopy. During subsequent assessments, this continued among patients in the sham group, whereas in the bronchial thermoplasty group, a larger proportion guessed correctly.

Two- and 5-year follow-up data on patients in the treatment group of the AIR2 trial have been published. In 2011, Castro et al reported 2-year data on 166 (87%) of 190 patients randomized to the bronchial thermoplasty group. In the second year after treatment, the proportion of participants who experienced severe exacerbations was 23.0% (95% confidence interval [CI], 16.6% to 29.5%). This compares with a 30.9% (95% CI, 24.2% to 37.7%) rate of exacerbations during year 1. The proportion who experienced asthma adverse events was 28.7% (95% CI, 22.1% to 35.3%) in year 1 and 26.5% (95% CI, 19.8 to 33.2) in year 2. In 2013, Wechsler et al reported 5-year data on 162 patients in the AIR2 trial (85% of those randomized to the treatment group). In a matched-pair analysis including the 162 study completers and the same group in previous years, the rate of severe exacerbations in years 1, 2, 3, 4, and 5 were 30.9%, 23.5%, 34.0%, 36.4%, and
21.6%, respectively. The proportion of patients experiencing severe exacerbations in years 2, 3, 4, and 5 did not differ significantly from the number of exacerbations in year 1. The proportion of patients who experienced asthma adverse events (at least ≥2 asthma symptoms occurring at the same time) were 28.7%, 27.9%, 29.6%, 31.4%, and 24.7%, respectively. The proportion of patients with at least 1 hospitalization for respiratory adverse events these same years was 3.3%, 4.2%, 6.2%, 5.7%, and 1.9%, respectively. In the 12 months before bronchial thermoplasty, the rate of hospitalization for respiratory symptoms in this group was 4.2%. These follow-up studies are limited in that follow-up data were not collected on patients randomized to the sham group, and therefore outcomes (e.g., rate of exacerbations, rate of hospitalizations) cannot be compared in patients who did and did not receive bronchial thermoplasty.

Systematic Reviews
Several pooled analyses of the 3 published RCTs were identified. Most recently, in 2016, Zhou et al published a systematic review of the published RCTs and extension studies, focusing on the durability and long-term responses for treated patients.11 Reviewers pooled data on long-term effects in bronchial thermoplasty–treated patients only (i.e., not in comparison groups). In an analysis of 216 patients with 5 years of follow-up, there was no significant decline in spirometry-detected prebronchodilator FEV1 (percent predicted) compared with 1-year findings (weighted mean difference [WMD], 0.75; 95% CI, -3.36 to 1.85; p=0.57; I²=0%). Similarly, there was no significant decline in postbronchodilator FEV1 (WMD=0.62; 95% CI, -3.32 to 2.08; p=0.65; I²=0%). In terms of adverse events over time, the rates of respiratory adverse events, emergency department visits for adverse events, and hospitalizations did not differ significantly after the 1- and 5-year follow-ups.

In 2014, a Blue Cross Blue Shield Association Technology Evaluation Center (TEC) Assessment was published on bronchial thermoplasty for treatment of inadequately controlled severe asthma.3 The Assessment included the 3 published RCTs discussed and concluded, “the evidence is insufficient to determine whether potential improvements in some outcomes, but not others defining the net health outcome, outweigh the potential harms” and that the technology did not meet TEC criteria.

In 2014, a Cochrane review of RCTs was published by Torrego et al.12 Reviewers included the 3 RCTs discussed herein. Potential trial limitations identified by reviewers were lack of blinding in 2 of the 3 trials and lack of a sham control in 2 trials. Pooled analyses were not conducted for asthma exacerbation outcomes. A meta-analysis of the 3 trials found significantly greater improvement in AQLQ scores at 12 months in the bronchial thermoplasty groups than in the control groups (mean difference [MD], 0.28; 95% CI, 0.07 to 0.40). However, at 12 months, the proportion of patients using rescue medication did not differ significantly between groups (MD = -0.68; 95% CI, -3.63 to 2.28). In terms of adverse events, a significantly higher number of patients were admitted to the hospital for respiratory events during the treatment period (relative risk [RR], 3.50; 95% CI, 1.26 to 9.68). There was no significant difference between groups in the proportion of patients admitted to the hospital for respiratory events in the posttreatment period (RR=1.12; 95% CI, 0.44 to 2.85).

Previously, in 2011, Wu et al published a meta-analysis of the findings of the 3 published RCTs.13 Pooled analyses of them found greater mean improvement in asthma QOL in the bronchial thermoplasty groups than in the control groups (WMD=0.63; 95% CI, 0.10 to 1.15) and greater improvement in the peak expiratory flow with bronchial thermoplasty treatment than with the control treatment (WMD=21.78; 95% CI, 8.06 to 35.50). During the treatment period (beginning on the day of the first treatment session and lasting 6 weeks after the last session), there were more respiratory adverse events in the bronchial thermoplasty groups (1113 events in 257 patients) than in the control groups (369 events in 164 patients) (p value not reported). Also during the treatment period, there was a significantly higher risk of hospitalization with bronchial thermoplasty than with control (RR=3.78; 95% CI, 1.39 to 10.24). In the posttreatment period (end of treatment to the 12-month follow-up visit), there was no significant difference between groups in the risk of hospitalization (RR=1.15; 95% CI, 0.47 to 2.79).
Case Series
After publication of the 3 RCTs (described above), several case series have described outcomes in clinical practice. They generally had small sample sizes (e.g., N=7,14 N=10,15 and N=2016). In addition, a rigorous U.K. registry study was published by Burn et al (2016), which focused on safety outcomes.17 The study combined data from 2 sources, the U.K. Difficult Asthma Registry and the Hospital Episode Statistics warehouse, and included patients treated with bronchial thermoplasty in the U.K. between June 2011 and January 2015. Eighty-three patients were identified in the Difficult Asthma Registry and 85 in the Hospital Episode Statistics database. For 59 patients, data in the 2 databases could be matched. Most patients had a course of 3 bronchial thermoplasty treatment sessions. Data from the matched cohort were used to calculate event rates for 4 binary safety outcomes. Procedural complications were reported in 17 (11%) of 152 procedures in 13 (22%) patients; emergency department readmissions within 30 days of the initial hospitalization were reported for 15 (11.8%) patients; and accident and emergency visits (i.e., emergency department) visits for any reason were reported for 13 (8.6%) patients. For the fourth binary outcome (postprocedure overnight stay), 70 (46.1%) of 152 procedures were followed by an overnight stay. In total, 20.4% of procedures in the matched cohort were associated with at least 1 of the 4 safety issues. The authors noted that the relatively high rate of safety events might be related to older patients with more severe disease being treated in clinical practice compared with patients included in clinical trials.

Section Summary: Bronchial Thermoplasty for the Treatment of Asthma
Three RCTs have evaluated bronchial thermoplasty for the treatment of asthma. The AIR2 trial is the largest RCT, and the only one double-blinded and sham-controlled, with sites in the United States. Over 1 year, bronchial thermoplasty was not found to be superior to sham treatment on the investigator-designated primary efficacy outcome of mean change in QOL score, but was found to be superior on a related outcome, improvement in quality of life of at least 0.5 points on the AQ6Q. There was a high response rate in the sham group of the AIR2 trial, which suggests a large placebo effect, particularly for subjective outcomes such as QOL. On the secondary outcomes, bronchial thermoplasty provided greater benefit than sham treatment on some, but not all, outcomes. In the AIR and RISA trials, there were improvements in QOL for the bronchial thermoplasty group compared to the medical management group. However, given the lack of benefit in the AIR2 trial, it is possible that the differences in QOL for these 2 trials were due at least in part to a placebo effect. There are no long-term sham-controlled efficacy data. Findings on adverse events from the 3 trials have suggested that bronchial thermoplasty is associated with a relatively high rate of adverse events, including hospitalizations during the treatment period, but not in the posttreatment period. Safety data up to 5 years have been reported in the RCTs for the patients treated with bronchial thermoplasty but not for control patients. Safety data from a U.K. registry study, published in 2016, found that 20% of bronchial thermoplasty procedures were associated with at least 1 of 4 safety events (i.e., procedural complications, emergency respiratory readmissions, emergency department visits, and/or postprocedure overnight stays).

Summary of Evidence
For individuals who have asthma refractory to standard treatment who receive bronchial thermoplasty, the evidence includes 3 randomized controlled trials (RCTs) and meta-analyses of these RCTs. Relevant outcomes are symptoms, quality of life, hospitalizations, and treatment-related morbidity. The AIR2 trial is the largest of the 3 published RCTs, and the only one double-blinded and sham-controlled, with sites in the United States. Over 1 year, bronchial thermoplasty was not found to be superior to sham treatment on the investigator-designated primary efficacy outcome of mean change in quality of life score, but was found to be superior on a related outcome, improvement in quality of life of at least 0.5 points on the Asthma Quality of Life Questionnaire. There was a high response rate in the sham group of the AIR2 trial, which suggests a large placebo effect, particularly for subjective outcomes such as quality of life. There are no long-term sham-controlled efficacy data. Findings on adverse events from the 3 trials have suggested that bronchial thermoplasty is associated with a relatively high rate of adverse events, including hospitalizations during the treatment period, but not in the posttreatment period.
period. Safety data up to 5 years have been reported in the RCTs for the patients treated with bronchial thermoplasty but not for control patients. Safety data from a U.K. registry study, published in 2016, found that 20% of bronchial thermoplasty procedures were associated with a safety event (i.e., procedural complications, emergency respiratory readmissions, emergency department visits, and/or postprocedure overnight stays). Conclusions cannot be drawn about the effect of bronchial thermoplasty on the net health outcome due to the limited amount of sham-controlled data (1 RCT) on short-term efficacy, the uncertain degree of treatment benefit in that single sham-controlled trial, the lack of long-term sham-controlled data in the face of a high initial placebo response, and the presence of substantial adverse events. In addition, there is a lack of data on patient selection factors for this procedure and, as a result, it is not possible to determine whether there are patient subgroups that might benefit. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Supplemental Information**

**Clinical Input from Physician Specialty Societies and Academic Medical Centers**

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

In response to requests from Blue Cross Blue Shield Association, input was received through 1 physician specialty society and 4 academic medical centers in 2014. Input was mixed on whether bronchial thermoplasty is considered investigational for the treatment of asthma; 3 reviewers agreed with this statement and 2 reviewers disagreed. Reviewers who disagreed tended to use bronchial thermoplasty in patients who had not responded to other treatments and who did not think there were treatment alternatives.

**Practice Guidelines and Position Statements**

**Global Initiative for Asthma**

Global Initiative for Asthma (GINA) is an international network of organizations and professionals with expertise in asthma. The group has been updating a report entitled *Global Strategy for Asthma Management and Prevention* annually since 2002; the most recent update was issued in 2017.\(^{18}\) The organization recommends stepped care for treatment of asthma. Step 1 consists of reliever inhaler use on an as-needed basis. Step 2 involves low-dose controller medication plus as-needed reliever medication. Step 3 includes 1 or 2 controllers plus as-needed reliever medication. In step 4, 2 or more controllers are used in addition to as-needed reliever medication. Step 5 involves higher level care and/or add-on treatment. According to the GINA document, options for add-on treatment in step 5 include bronchial thermoplasty for some adults with severe asthma, anti-immunoglobulin E, sputum-guided treatment, add-on low-dose oral corticosteroids, and tiotropium. The document noted that evidence on bronchial thermoplasty is limited and long-term treatment effects are unknown.

**European Respiratory Society and American Thoracic Society**

In 2014, a joint task force of the European Respiratory Society and American Thoracic Society published guidelines on the definition, evaluation, and treatment of severe asthma.\(^{19}\) The guidelines were based on a systematic review of the literature. It includes the statement: “We recommend that bronchial thermoplasty is performed in adults with severe asthma only in the context of an Institutional Review Board approved independent systematic registry of a clinical study.” The authors remarked: “This is a strong recommendation, because of the very low confidence in the available estimates of effects of bronchial thermoplasty in patients with severe asthma.”

**American College of Chest Physicians**

As of March 2014, the American College of Chest Physicians (ACCP) had not addressed bronchial thermoplasty in any of its national guidelines. In May 2014, ACCP posted a position
statement on coverage and payment for bronchial thermoplasty.20 The document stated in part:

“…bronchial thermoplasty offers an important treatment option for adult patients with severe asthma who continue to be symptomatic despite maximal medical treatment and, therefore should not be considered experimental. Randomized controlled clinical trials of bronchial thermoplasty for severe asthma have shown a reduction in the rate of severe exacerbations, emergency department visits, and days lost from school or work. Additionally, data published in December, 2013 demonstrates the persistence of the reduction in asthma symptoms achieved by bronchial thermoplasty for at least 5 years...”

**British Thoracic Society and Scottish Intercollegiate Guidelines Network**

In 2014, the British Thoracic Society and the Scottish Intercollegiate Guidelines Network published revised national guidelines on management of asthma.21 The guidelines stated: “Bronchial thermoplasty may be considered for the treatment of adult patients who have poorly controlled asthma despite optimal therapy.” The guidelines included a summary of recommended stepwise management of asthma in adults. Bronchial thermoplasty is not specifically mentioned in the stepwise management summary, but step 5 includes recommendations to consider other treatments to minimize the use of steroid tablets and to refer patients for specialty care.

**National Institute for Health and Care Excellence**

In 2012, the National Institute for Health and Care Excellence published guidance on bronchial thermoplasty for severe asthma.22 The guidance stated: “Evidence on the efficacy of bronchial thermoplasty for severe asthma shows some improvement in symptoms and quality of life, and reduced exacerbations and admission to hospital. Evidence on safety is adequate in the short and medium term. More evidence is required on the safety of the procedure in the long term. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.”

**U.S. Preventive Services Task Force Recommendations**

Not applicable.

**Medicare National Coverage**

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

**Ongoing and Unpublished Clinical Trials**

Some currently unpublished trials that might influence this review are listed in Table 1.

<table>
<thead>
<tr>
<th>NCTNo.</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>NCT02225392a</td>
<td>Unravelling Targets of Therapy in Bronchial Thermoplasty in Severe Asthma (TASMA)</td>
<td>40</td>
<td>Apr 2018</td>
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<tr>
<td>NCT02464995</td>
<td>Bronchial Thermoplasty in Severe Asthma With Frequent Exacerbations (THERMASCORT)</td>
<td>34</td>
<td>Nov 2018</td>
</tr>
<tr>
<td>NCT02104856a</td>
<td>Bronchial Thermoplasty Global Registry (BTRegistry)</td>
<td>160</td>
<td>Jun 2019</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

a Denotes industry-sponsored or cosponsored trial.

**References**

3. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). Bronchial thermoplasty for treatment of inadequately controlled severe asthma. TEC Assessments. 2014;Volume 29:Tab 12. PMID 25962190

Documentation for Clinical Review

- No records required

Coding

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

IE

The following services may be considered investigational.

<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT®</td>
<td>31660</td>
<td>Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with bronchial thermoplasty, 1 lobe</td>
</tr>
<tr>
<td></td>
<td>31661</td>
<td>Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with bronchial thermoplasty, 2 or more lobes</td>
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<tr>
<td>HCPCS</td>
<td>None</td>
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</tr>
<tr>
<td>ICD-10 Procedure</td>
<td>0B538ZZ</td>
<td>Destruction of Right Main Bronchus, Via Natural or Artificial Opening Endoscopic</td>
</tr>
<tr>
<td></td>
<td>0B548ZZ</td>
<td>Destruction of Right Upper Lobe Bronchus, Via Natural or Artificial Opening Endoscopic</td>
</tr>
<tr>
<td></td>
<td>0B558ZZ</td>
<td>Destruction of Right Middle Lobe Bronchus, Via Natural or Artificial Opening Endoscopic</td>
</tr>
<tr>
<td></td>
<td>0B568ZZ</td>
<td>Destruction of Right Lower Lobe Bronchus, Via Natural or Artificial Opening Endoscopic</td>
</tr>
<tr>
<td></td>
<td>0B578ZZ</td>
<td>Destruction of Left Main Bronchus, Via Natural or Artificial Opening Endoscopic</td>
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<tr>
<td></td>
<td>0B588ZZ</td>
<td>Destruction of Left Upper Lobe Bronchus, Via Natural or Artificial Opening Endoscopic</td>
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<tr>
<td></td>
<td>0B598ZZ</td>
<td>Destruction of Lingula Bronchus, Via Natural or Artificial Opening Endoscopic</td>
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<tr>
<td></td>
<td>0B5B8ZZ</td>
<td>Destruction of Left Lower Lobe Bronchus, Via Natural or Artificial Opening Endoscopic</td>
</tr>
<tr>
<td>ICD-10 Diagnosis</td>
<td>All Diagnoses</td>
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</table>

Policy History

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

<table>
<thead>
<tr>
<th>Effective Date</th>
<th>Action</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>01/06/2012</td>
<td>BCBSA Medical Policy adoption</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>03/13/2012</td>
<td>Coding Update</td>
<td>Administrative Review</td>
</tr>
<tr>
<td>02/22/2013</td>
<td>Coding Update</td>
<td>Administrative Review</td>
</tr>
</tbody>
</table>
### Effective Date | Action | Reason
---|---|---
11/26/2014 | Policy revision without position change | Medical Policy Committee
08/01/2016 | Policy revision without position change | Medical Policy Committee
08/01/2017 | Policy revision without position change | Medical Policy Committee

### Definitions of Decision Determinations

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

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

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

### Prior Authorization Requirements (as applicable to your plan)

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

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

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