

<b>MEDICAL POLICY</b>	<b>Bronchial Thermoplasty</b>
<b>Effective Date: 7/1/2021</b>  7/1/2021	Medical Policy Number: 8 Technology Assessment Committee Approved Date: 6/10; 1/14; 4/15; 12/15 Medical Policy Committee Approved Date: 11/11; 1/13; 11/16; 1/18; 2/19; 3/2020; 5/2020; 6/2021
Medical Officer	Date

**See Policy CPT CODE section below for any prior authorization requirements**

**SCOPE:**

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as “Company” and collectively as “Companies”).

**APPLIES TO:**

All lines of business

**BENEFIT APPLICATION**

Medicaid Members

*Oregon:* Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

**POLICY CRITERIA**

I. Bronchial thermoplasty is considered **not medically necessary and is not covered** as a treatment of any condition, including, but not limited to, asthma.

Link to [Policy Summary](#)

**CPT CODES**

All Lines of Business	
Not Covered	
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

## DESCRIPTION

### Asthma

Asthma is a chronic disorder causing inflammation of the airways resulting in impaired breathing due to airflow obstruction, bronchial hyperresponsiveness, and underlying inflammation.<sup>1</sup> According to the American Thoracic Society (ATS) and European Respiratory Society (ERS), “severe asthma is asthma requiring treatment with high-dose inhaled corticosteroids plus a second controller medication (and/or systemic corticosteroids) to maintain asthma control. Additionally, patients who had required systemic corticosteroids for  $\geq 50\%$  of the previous year are also classified as having severe asthma.”<sup>1,2</sup> Standard treatment for severe asthma includes a combination of high-dose inhaled glucocorticoid and an inhaled, long-acting  $\beta 2$ -agonist (LABA). In patients who do not achieve acceptable asthma control despite high dosages of medication, add-on therapies including LABAs, leukotriene modifiers, theophylline, or omalizumab may be included in the treatment regimen.

### Bronchial Thermoplasty

The goal of bronchial thermoplasty (BT) is to reduce the smooth muscle that constricts airways during asthma attacks.<sup>1</sup> The procedure involves the insertion of a catheter with an expandable electrode array into the airway via bronchoscope. This catheter is attached to a radiofrequency generator, which then sends an electrical current to the electrodes inside the airway. The electrodes are held against the bronchial walls and the electrical current generates heat that destroys the smooth muscle underneath the lining of the bronchial passages. “Bronchial thermoplasty is performed in 3 separate procedures (i.e., 3 sessions to complete the treatment) in which all accessible airways located beyond the mainstream bronchi (average of 3 to 10 mm in diameter), except for the right middle lobe, are treated.”<sup>1</sup> In order to decrease procedure time and the risk of widespread irritation, there is a recovery period of at least 3 weeks between BT sessions.

## REVIEW OF EVIDENCE

A review of the ECRI, Hayes, Cochrane, and PubMed databases was conducted regarding the use of bronchial thermoplasty as a treatment for asthma. Below is a summary of the available evidence identified through March 2021.

### Bronchial Thermoplasty

#### Systematic Reviews

- In 2020, ECRI conducted a systematic review evaluating the safety and efficacy of the Alair Bronchial Thermoplasty (BT) System for treating severe asthma.<sup>3</sup> Investigators searched the literature through May 12, 2020. In total, 2 systematic reviews and 1 prospective, nonrandomized study. One systematic review with meta-analysis (3 RCTs, Alair n = 288 and omalizumab immunotherapy n = 1,267) made indirect comparisons between Alair and immunotherapy and reported on severe asthma exacerbations, hospitalizations, ED visits, and QOL up to 1-year follow-up in patients with severe asthma. An additional systematic review assessed 12 studies (n= 386) assessed the same

outcomes of interest at 1-year follow-up in patients with moderate to severe asthma treated as usual, with or without BT, or a sham procedure. Authors also reported on 5-year follow-up after BT.

One RCT (AIR2 trial) included for review reported no differences in Asthma Control Questionnaire (ACQ) scores, Asthma Quality of Life Questionnaire (AQLQ) scores, asthma-related hospitalizations, and rescue medication use at 1-year follow-up. Patients had fewer severe exacerbations (requiring systemic or double-dose inhaled corticosteroids) at 1-year follow-up with BT, however the clinical significance of this difference was unclear. Bronchial thermoplasty resulted in more hospitalizations after 6 weeks (8.4% versus 2%) but fewer emergency department (ED) visits at 1 year (15.3% versus 8.4% of patients). Two RCTs (AIR and RISA) reported improved ACQ and AQLQ scores at 1-year follow-up with BT compared with standard care alone; however, the between-group differences are of unclear clinical significance. Authors also reported more asthma-related hospitalizations at 12-week follow-up with BT (27% versus 0%). A meta-analysis of 3 RCTs found no differences in AQLQ scores, hospitalizations, or severe exacerbations at up to 1-year follow-up between standard care with BT or omalizumab. However, authors found 33% more exacerbations with BT when the 6-week peri-procedural period was included ( $p = 0.009$ ). Authors reported fewer ED visits with BT (risk ratio = 0.25, 95% CI: 0.07 to 0.91,  $p = 0.04$ ). One nonrandomized comparison study (Langton et al. 2020) reported no differences in ACQ scores, exacerbation rates, or rescue medication use at up to 1-year follow-up between BT and mepolizumab. The systematic review that included adverse events reported no differences in respiratory-related hospitalizations or ED visits between 1- and 5-year follow-up and no deaths up to 5-year follow-up. Adverse events included hemoptysis (17%), atelectasis (13%), chest discomfort (8%), wheezing (8%), lower respiratory tract infection requiring hospitalization (7%), and lung abscess (3%) up 5-year follow-up.

Investigators concluded that evidence evaluating the Alair System was “inconclusive.” Limitations in studies published to date included small sample sizes, lack of blinding, and differences in duration of group follow-ups, and nonparallel follow-up, and diverse patient selection criteria.

- In 2016 (reviewed in 2020), Hayes conducted an evidence review to evaluate the use of bronchial thermoplasty (BT) to treat asthma.<sup>1</sup> The evidence review identified seven studies in 11 publications, including 1 good-quality randomized controlled trial (RCT), 2 fair-quality RCTs, 1 very-poor-quality retrospective cohort study, and 3 very-poor-quality case series. All included studies evaluated bronchial thermoplasty as an adjunct to conventional drug treatment. Sample sizes varied from 8 to 288 patients and follow-up times included 1 year of controlled follow-up in 3 RCTs and 5 years of uncontrolled follow-up in 2 RCTs. Outcomes of interest included asthma-related quality of life (ARQOL), exacerbations, asthma symptoms, medication use, hospitalization, emergency department (ED) visits, lung function, respiratory parameters, and adverse events (AEs).

There was inconsistent evidence regarding the rate of severe exacerbations following BT. One RCT found that severe exacerbation in the BT group decreased at 1 year; however, another RCT found no difference between-groups at 1-year follow-up. Of 3 RCTs that evaluated asthma symptoms, only 1 found that BT improved asthma symptoms at 1 year. Additionally, all 3 RCTs found that the FEV<sub>1</sub> did not improve in the BT group compared to the control group. Lastly, 2 of 3 RCTs found that ARQOL was improved at 1-year follow-up in the BT group. In regards to hospitalizations, “(o)ne RCT found that significantly more bronchial thermoplasty patients compared with control patients were hospitalized during the treatment period. At 1-year follow-up, an RCT found that hospitalizations in the thermoplasty group did not decrease compared

with the control group.”<sup>1</sup> During the treatment period, BT was associated with a statistically significant increase in “dyspnea (60% to 71% of thermoplasty patients), wheezing (50% to 73%), chest discomfort (40% to 56%), night awakenings (40%), sputum discoloration (11% to 33%), cough (53% to 94%), productive cough (40% to 53%), bronchial irritation (9% to 13%), and nasal congestion (13% to 20%).”<sup>1</sup> Furthermore, the Hayes evidence review concluded insufficient evidence to establish the long-term efficacy of BT for asthma.

Hayes rated the overall body of evidence evaluating BT for asthma to be, “small in size and low in quality.”<sup>1</sup> This quality rating was due to inconsistent results regarding short-term benefits, varied patient selection, poor quality and subsequent high risk of bias of included studies, small quantity of available RCTs, and insufficient evidence concerning the long-term efficacy of BT. “Limitations of individual studies included a lack of control or comparator group, lack of sham control, small sample size, moderate-to-high loss to follow-up, use of self-reported data collected in daily diaries that may be subject to recall bias (e.g., rescue medication use, asthma symptoms and exacerbations, peak expiratory flow), and lack of controlled follow-up after 1 year.”<sup>1</sup>

Hayes concluded that in the first year following BT treatment the evidence indicates improved asthma-related quality of life, symptoms relief, reduced medication use, and reduction in ED visits. However, BT did not reduced hospitalization during the treatment period and there was no evidence of improved lung function (e.g., FEV<sub>1</sub>). Ultimately, Hayes gave the following ratings:

- C (potential but unproven benefit)— For bronchial thermoplasty for severe, persistent asthma in adult patients (18 years or older) whose asthma has not been well controlled by long-acting bronchodilators and glucocorticoids. This Rating reflects a small body of low-quality evidence, which suggests some positive but inconsistent results regarding short-term benefits of bronchial thermoplasty. This Rating also reflects the insufficient evidence concerning the long-term safety and efficacy of bronchial thermoplasty.
  - D2 (insufficient evidence)— For bronchial thermoplasty for mild-to-moderate asthma in adults. This Rating reflects the paucity of data evaluating bronchial thermoplasty in patients who meet these criteria.
  - D2 (insufficient evidence)— For bronchial thermoplasty for pediatric patients. This Rating reflects the paucity of data evaluating bronchial thermoplasty in patients younger than 18 years of age.<sup>1</sup>
- In 2017, the Agency for Healthcare Research and Quality (AHRQ) conducted a systematic review evaluating the safety and efficacy of bronchial thermoplasty (BT) in adults with asthma.<sup>4</sup> Investigators systematically searched the literature through April 2017, extracted data, and assessed study quality using the Cochrane Risk of Bias instrument, and according to the methods guidance established by the Evidence-based Practice Center program. Expert peer reviewers were enlisted to review and comment on the draft report and suggested revisions that were incorporated into the final report. The review’s key question was: “what are the benefits and harms of using BT in addition to standard treatment for the treatment of adult (≥18 years) patients with asthma?”<sup>4</sup>

In total, 15 studies were included for review (3 RCTs (n=432) and 9 observational studies (n=55)). Compared to standard care, investigators judged the strength of evidence to be “low” for reported improvements among BT patients in asthma control, quality of life, mild exacerbations, pulmonary physiology measures, the use of rescue medication and the number of hospitalizations. Among all

reported outcomes, investigators judged the evidence to be “moderate” solely for reductions in the number of emergency room visits for patients treated with BT. Adverse events were common among BT patients (e.g. bronchial irritation, chest discomfort, coughing, wheezing); serious adverse events were less frequent, but reported in six case reports and two small case series. Investigators also noted that populations in included studies were highly selected and heterogeneous, further limiting results’ generalizability. Reviewers concluded that “the available body of literature on BT is small and uncertainty remains about appropriate patient selection criteria and the effects of the treatment beyond 5 years.”<sup>4</sup>

- In 2017, Niven et al. conducted a systematic review and indirect treatment comparison (ITC) of bronchial thermoplasty (BT) versus omalizumab (OM) for the treatment of uncontrolled severe asthma.<sup>5</sup> Independent reviewers systematically identified eligible studies, assessed quality, and extracted data. The primary outcomes of interest were the rate ratios (RRs) of severe asthma exacerbations and asthma exacerbation-related events (e.g., hospitalizations, emergency department [ED] visits, and unscheduled doctor’s office visits), and change in total score on the asthma-related quality-of-life questionnaire (AQLQ).

Following systematic review, 7 randomized controlled trials (RCTs) were identified as eligible for inclusion. Of these 7 trials, one sham-controlled trial of BT and two placebo-controlled trials of OM were included in the ITC. When using ITC to evaluate the post-treatment period of the respective trials, there was a statistically significant difference in favor of BT for asthma-related ED visits. However, there was no statistically significant difference between BT and OM for severe asthma exacerbations, asthma-related hospitalizations, and unscheduled doctor’s office visits. In using ITC to evaluate events occurring during the treatment period, there was no statistically significant difference between BT and OM for asthma-related hospitalizations and ED visits; however, there was a statistically significant difference in favor of OM for severe asthma-related exacerbations. The indirect comparison of quality of life outcomes shows similar results for both OM and BT.

Strengths of this systematic review include the gathering of evidence, assessment of quality, and extraction of data by several independent reviewers. Limitations are present due to the use of indirect treatment comparison analysis, which is subject to considerable biases and lacks the robustness of a traditional meta-analysis. The authors also identified significant differences in the baseline characteristic of subjects across trials, further impacting the validity of the ITC. Financial or sponsorship bias is also probable due to the study being funded by the manufacturer of the BT device (Boston Scientific Corp.). The authors concluded that BT compares well with other, potentially more costly, pharmacotherapy treatments for asthma. However, the authors state, “the ITC should be interpreted cautiously considering the differences between patient populations in the included trials.”<sup>5</sup> Furthermore, the authors acknowledge that “the findings of this ITC are best considered indicative rather than definitive, in the absence of RCT evidence which directly compares BT and OM or which allows and indirect or mix treatment comparison in more comparable severe asthma populations.”<sup>5</sup>

- In 2016, Zhou et al. conducted a systematic review and meta-analysis to evaluate the long-term efficacy and safety of bronchial thermoplasty (BT) in patients with moderate-to-severe persistent asthma.<sup>6</sup> Independent reviewers systematically identified eligible studies, assessed quality, and extracted data. The primary outcomes of interest included spirometric data (e.g., FEV<sub>1</sub>), adverse respiratory events, and emergency room (ER) visits and hospitalization for respiratory illness.

Following systematic review, the authors identified 3 randomized controlled trials (RCTs) and their subsequent extension studies as eligible for inclusion. This included 249 BT-treated patients with 1-year follow-up (V1); whereas 216 of these patients completed 5-year follow-up (V5). Overall, most BT treated patients had a reduction in the usage of inhaled corticosteroids (ICS) and long-acting  $\beta_2$ -agonists (LABAs) (range: 12% to 49% reductions). There was also no evidence of significant decline in pre- or post-bronchodilator FEV<sub>1</sub> between V1 and V5; suggesting that BT might prevent rapid deterioration in lung function in severe asthmatic patients. Between V1 and V5 there was no statistically significant decrease in adverse respiratory events or ER visits for respiratory events. During the V1 to V5 period, no statistically significant increase was found in the incidence of hospitalizations for respiratory adverse events; however, the authors stated, “the frequency of respiratory adverse events should not be neglected during the early stage of BT intervention.”<sup>6</sup>

Strengths of this study include the gathering of evidence, assessment of quality, and extraction of data by several independent reviewers and the assessment of heterogeneity. However, the reliability of conclusions drawn from this study is hindered due to several limitations. These include, but are not limited to, the following:

- poor-to-fair methodological quality of included studies
- almost all studies included did not have a control/sham group for the 5-year follow-up
- probable publication bias due to the small number of selected studies
- two of the three selected studies took place outside of the United States
- meta-analysis was conducted inappropriately due to significant between-study heterogeneity, and no statistical methods were used to account for this heterogeneity

The authors concluded that BT shows “reasonable long-term safety and efficacy for moderate-to-severe asthmatic patients.”<sup>6</sup> However, the authors also suggest that “a large scale clinical study should be performed for confirming this finding.”<sup>6</sup>

- In 2014, Torrego and colleagues conducted a Cochrane systematic review to determine the efficacy and safety bronchial thermoplasty (BT) for moderate or severe persistent asthma in adults.<sup>7</sup> Independent reviewers systematically identified eligible studies, assessed quality, and extracted data. Study authors were also contacted, if necessary, for additional information or data. The outcomes of interest were quality of life, asthma exacerbations, and adverse events. The authors identified 3 randomized controlled trials (RCTs) encompassing 429 patients as eligible for inclusion. Two RCTs compared BT with standard medical management and one RCT compared BT with a sham intervention. The pooled analysis showed improvement of quality of life at 12 months in BT patients; however, this did not reach the threshold for clinical significance. Furthermore, measurement of asthma symptom control showed no significant differences in all three trials. Two of the three trials showed a lower rate of exacerbation after 12 months in patients who underwent BT. One trial showed a statistically significant reduction in the proportion of patients visiting the emergency department for asthma-related adverse events. However, the trials showed no significant improvement in pulmonary function parameters and BT patients had a greater risk of hospitalization for respiratory adverse events during the treatment period. The risk of bias for these outcomes was determined to be high because two of the three studies did not have a sham intervention for the control group.

This Cochrane systematic review was of very good quality and had several strengths, including:

- the gathering of evidence, assessment of quality, and extraction of data by several independent reviewers
- contacting authors of selected studies for additional information or data
- assessment of heterogeneity and publication bias
- meta-analyses only being conducted when studies were determined to be homogeneous with respect to population, treatment, and outcome measures
- sensitivity analyses to evaluate the influence of studies with a high risk of bias or high losses to follow-up

Limitations of this systematic review are seen in the inclusion of studies with a high risk of bias and the potential for publication bias. Ultimately, the authors concluded that BT for patients with moderate to severe asthma provides modest clinical benefit in quality of life and exacerbations. However, these findings are at risk of bias because the main benefits were seen in the two trials that did not include a sham treatment. The authors suggested “further research should provide better understanding of the mechanisms of action of bronchial thermoplasty, as well as its effect in different asthma phenotypes or in patients with worse lung function.”<sup>7</sup>

#### Randomized Controlled Trials

- Two recent randomized controlled trials sought to evaluate the efficacy of bronchial thermoplasty for the treatment of severe asthma.<sup>8,9</sup> Both studies noted improvements in asthma quality of life questionnaire scores at follow-up among patients receiving treatment. Validity was limited by these studies’ small sample sizes (n=20 to 40) and lack of long-term follow-up (3 to 6 months).
- Three additional randomized controlled trials (RCTs) were identified which evaluated bronchial thermoplasty for the treatment of severe asthma.<sup>10-12</sup> All RCTs were included in one or more of the systematic reviews described above.

#### Nonrandomized Studies

- In 2017, Chupp et al. conducted an indirect treatment comparison (ITC) of two prospective multi-center studies to evaluate the long-term (3-year) outcomes of bronchial thermoplasty (BT) in patients with severe asthma.<sup>13</sup> The authors compared the results of the Asthma Intervention Research 2 (AIR2) (randomized, sham-controlled) trial with the Post-FDA Approval Clinical Trial Evaluating Bronchial Thermoplasty in Severe Persistent Asthma (PAS2)(prospective, open-label, observational). The first 190 patients in the PAS2 trial were compared with 190 BT-treated subjects in the AIR2 trial after 3 years of follow-up. Outcomes of interest included medication usage, severe exacerbations, emergency department visits for respiratory symptoms, hospitalizations, and lung function.

Patients in the PAS2 trial showed a significant reduction in inhaled corticosteroids (ICS) and oral corticosteroids (OCS), while subjects in the AIR2 trial only showed a significant reduction in ICS usage. Patients in both trials also showed a reduction in severe exacerbations when compared to the 12 months prior to treatment. Both trials showed a relative decrease in emergency department

visits and hospitalizations for respiratory symptoms. However, both trials showed no effect on spirometric parameters of lung function following BT.

Although this study shows a possible efficacious treatment for severe, persistent asthma, the results should be interpreted cautiously due to significant limitations. The indirect comparison between the AIR2 trial and the PAS2 trial is significantly limited due to cross-trial differences in the study design (randomized controlled trial versus nonrandomized observational trial) and use of a control/sham treatment arm. The validity of an ITC depends on the similarity of the trials involved; therefore, the comparison of these dissimilar trials produces significant bias and confounding factors which cannot be controlled for in statistical analyses. Ultimately, the authors concluded that the PAS2 trial produced similar results to the AIR2 trial in asthma control after BT. However, the authors stated that “further subgroup analysis is needed to help identify which asthma subjects are most likely to benefit from the bronchial thermoplasty procedure in the ‘real-world’.”<sup>13</sup>

- Additional nonrandomized studies were identified that evaluated the use of bronchial thermoplasty for severe asthma.<sup>14-17</sup> All studies were included in the Hayes evidence review described above; therefore, they will not be summarized here.

## Safety

### *Treatment-Related Safety*

Three studies (2 randomized controlled trials and 1 case series) reported on bronchial thermoplasty (BT) treatment-related safety.<sup>11,12,16</sup> During the treatment period, BT was associated with statistically significant increases in the following:

- dyspnea (60% to 71%)
- wheezing (50% to 73%)
- chest discomfort (40% to 56%)
- night awakenings (40%)
- sputum discoloration (11% to 33%)
- cough (53% to 94%)
- productive cough (40% to 53%)
- bronchial irritation (9% to 13%)
- nasal congestion (13% to 20%)

Furthermore, seven studies reported a statistically significant increase in respiratory-related hospitalization during the BT treatment period.<sup>10-12,14-17</sup>

### *Safety During Longer-Term (5-Year) Follow-Up*

- In 2011, Thomson et al. reported 5-year follow-up data for patients enrolled in the Cox et al. (2006) RCT.<sup>16,18</sup> Complications occurring from 1 to 5 years following bronchial thermoplasty (BT) were reported for 45 of 109 patients in the treatment group and from years 1 to 3 for 24 of 109 patients enrolled in the control group. An increase in the average number of events of worsening asthma occurred during the first year following treatment than in subsequent years. In the BT group, hospitalizations occurred in 7% of patients in the first two years and in 2 percent of patients during

years 3 through 5. Conversely, in years 1-2 and year 3 the control patients experienced 0% and 5% hospitalizations, respectively. Emergency department (ED) visits were seen in 4% of BT patients during year 1 and 2-7% of patients during years 2 through 5. ED visits occurred in 0%, 5%, and 13% of control patients during years 1, 2, and 3, respectively. There were no statistically-significant differences between the BT and control groups for worsening of asthma, hospitalizations, and ED visits. During the 5 years of follow-up, no BT patients had pneumothorax, required mechanical ventilation, or died due to thermoplasty.

- In 2013, Pavord et al. conducted an uncontrolled follow-up of patients enrolled in Pavord et al. (2007) to assess the long-term safety of bronchial thermoplasty (BT).<sup>12,19</sup> The analysis included 14 patients with 5-year follow-up data. In years 2 to 5, rates of respiratory AEs, respiratory-related hospitalizations, and emergency department visits were unchanged.
- In 2013, Wechsler et al. conducted an uncontrolled 5-year follow-up of the bronchial thermoplasty (BT) patients enrolled in the Castro et al. (2010) RCT.<sup>10,20</sup> A total of 162 (85.3%) of 190 BT-treated subjects were available for 5-year follow-up. The rate of subjects experiencing severe exacerbations and emergency department visits remained less than pre-BT treatment through years 1 to 5. Pre-bronchodilator FEV<sub>1</sub> values remained consistent through years 1 to 5. However, respiratory adverse events and respiratory-related hospitalizations remained unchanged through 5 years.

## CLINICAL PRACTICE GUIDELINES

### National Institute for Health and Care Excellence (NICE)

In 2018, NICE published an interventional procedures guidance addressing the use of bronchial thermoplasty (BT) in the treatment of severe asthma.<sup>21</sup> In reviewing the same studies as the AHRQ study discussed above,<sup>4</sup> NICE concluded that evidence evaluating the safety and efficacy of BT was adequate. NICE stated that the BT treatment should only be administered by a multidisciplinary team in a specialist center with access to an intensive care unit. The committee also concluded that patient selection criteria remained unclear, and that BT should be reserved for patients with severe asthma who have failed to respond to optimal drug treatment.

### Global Initiative for Asthma (GINA)

The 2020 GINA report for the global strategy for asthma management and prevention gave the following recommendations regarding bronchial thermoplasty:

- Bronchial thermoplasty is a potential treatment option at Step 5 (higher level care and/or add-on treatment) in some countries for adult patients whose asthma remains uncontrolled despite optimized therapeutic regimens and referral to an asthma specialty center. Evidence B.<sup>22</sup>
  - GINA defines evidence B as a limited body of data including meta-analyses and randomized controlled trials (RCTs). "Evidence is from endpoints of intervention studies that include only a limited number of patients, post hoc or subgroup analysis of RCTs or meta-analysis of such RCTs. In general, Category B pertains when few randomized trials exist, they are small in size, they were under-taken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent."<sup>22</sup>

- The GINA report also states that the bronchial thermoplasty treatment is associated with a large placebo effect. Furthermore, “bronchial thermoplasty was associated with an increase in asthma exacerbations during the 3 month treatment period, and a subsequent decrease in exacerbations, but no beneficial effect on lung function or asthma symptoms compared with sham-controlled patients.”<sup>22</sup>
- GINA concludes that additional longer-term follow-up of larger cohorts comparing effectiveness and safety in both active and sham-controlled patients and that caution should be used in selecting patients for bronchial thermoplasty.

The recommendations made by GINA were not based on a systematic review of the evidence. Furthermore, authors did not use a standardized grading system (e.g., the Grading of Recommendations Assessment, Development and Evaluation [GRADE] approach) for evaluating the quality of the included evidence.

#### Agency for Healthcare Research and Quality (AHRQ)

The 2017 AHRQ report on the “Effectiveness and safety of bronchial Thermoplasty in Management of Asthma” concludes:

- BT along with standard medical management, compared to medical management alone, may improve asthma control and quality of life, but evidence is insufficient to determine impact on asthma exacerbations.
- BT along with standard medical management, compared to a similar procedure without the heat (sham procedure), does not improve asthma control or hospitalizations but may reduce severe exacerbations and emergency room visits.
- BT causes more adverse events (such as worsening of asthma symptoms, respiratory infections, and coughing up blood) during the treatment period than standard treatment. Based on the available literature, there is still uncertainty about the balance of benefits and harms, and about which patients are most likely to benefit from the procedure.

#### American Thoracic Society/European Respiratory Society (ATS/ERS)

The 2014 evidence-based ATS/ERS international guideline for the definition, evaluation, and treatment of severe asthma gave the following recommendations regarding bronchial thermoplasty:

- “The Guideline Committee recommends that bronchial thermoplasty is performed in adults with severe asthma only in the context of an Institutional Review Board-approved independent systematic registry or a clinical study (strong recommendation, very low quality evidence).
- This recommendation places a higher value on avoiding adverse effects and on increased use of resources, and on a lack of understanding of which patients may benefit, and a lower value on the uncertain improvement in symptoms and quality of life.
- This is a strong recommendation, because of the very low confidence in the currently available estimates of effects of bronchial thermoplasty in patients with severe asthma. Both potential benefits and harms may be large and the long-term consequences of this new approach to asthma therapy utilizing an invasive physical intervention are unknown. Specifically designed studies are needed to define its effects on relevant objective primary outcomes such as exacerbation rates, and on long-term effects on lung function. Studies are also needed to better understand the phenotypes of responding patients, its effects in patients with severe obstructive asthma (forced expiratory

volume in 1 second [FEV1] <60% of predicted value) or in whom systemic corticosteroids are used, and its long-term benefits and safety. Further research is likely to have an important impact on this recommendation.”<sup>2</sup>

#### American College of Chest Physicians (ACCP)

In 2014, the ACCP released a position statement on the coverage and payment for bronchial thermoplasty.<sup>23</sup> This position statement supports the use of bronchial thermoplasty in patients with severe asthma who continue to be symptomatic despite maximal medical treatment; however, this statement is based on clinical consensus and not a systematic review of the evidence.

## CENTERS FOR MEDICARE & MEDICAID

As of 4/12/2021, no Centers for Medicare & Medicaid (CMS) coverage guidance was identified which addresses bronchial thermoplasty as a treatment of asthma. A review of Medicare databases identified CMS Transmittal 2234 and MLN Matters Number MM7443<sup>24,25</sup>; however, these do not constitute coverage guidance. Therefore, the commercial criteria above will apply to Medicare members.

## POLICY SUMMARY

There is not enough evidence to support the use of bronchial thermoplasty (BT) for the treatment of severe, drug-refractory asthma. It is currently unknown whether BT improves long-term health outcomes. Furthermore, the long-term safety of BT remains unclear. The only available long-term safety data is of low quality and based on very small patient populations. Ultimately, reliable conclusions cannot be drawn regarding the safety and efficacy of BT for the treatment of severe asthma. Additionally, there are no U.S.-based clinical practice guidelines supported by a systematic review of the evidence that recommend BT for the treatment of severe, drug-refractory asthma. While the National Institute for Health and Care Excellence (NICE) considers the evidence base sufficient to support the use of BT, the Agency for Healthcare Research, having assessed the same publications as NICE, judged the standard of evidence to be “low” or “insufficient” for most reported outcomes.

## INSTRUCTIONS FOR USE

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

**REGULATORY STATUS**

U.S. Food and Drug Administration (FDA)

The U.S. FDA approved the Alair Bronchial Thermoplasty System (Boston Scientific Corp.) under the premarket approval (PMA) process as a class III (high-risk) device on April 27, 2010. PMA # P080032.<sup>26</sup>

Device Name & Manufacturer	Indications for Use	Contraindications for Use
<p>Alair® Bronchial Thermoplasty System by Boston Scientific Corp.</p>	<p>The treatment of severe persistent asthma in patients 18 years of age and older whose asthma is not well controlled with inhaled corticosteroids and long acting beta agonists.</p>	<p>Patients with the following conditions should not be treated:</p> <ul style="list-style-type: none"> <li>• Presence of a pacemaker, internal defibrillator, or other implantable electronic devices</li> <li>• Known sensitivity to medications required to perform bronchoscopy, including lidocaine, atropine, and benzodiazepines</li> <li>• Patients previously treated with the Alair® System should not be retreated in the same area(s). No clinical data are available studying the safety and/or effectiveness of repeat treatments.</li> </ul> <p>Patients should not be treated while the following conditions are present:</p> <ul style="list-style-type: none"> <li>• Active respiratory infection,</li> <li>• Asthma exacerbation or changing dose of systemic corticosteroids for asthma (up or down) in the past 14 days,</li> <li>• Known coagulopathy,</li> <li>• As with other bronchoscopic procedures, patients should stop taking anticoagulants, antiplatelet agents, aspirin and NSAIDS before the procedure with physician guidance</li> </ul>

Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical

necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

## REFERENCES

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