Washington State Health Care Authority
Health Technology Assessment

Bronchial Thermoplasty for Asthma

Findings & Decision
Timeline and Overview of Comments

The Health Technology Assessment (HTA) program received comments in response to the posted Health Technology Clinical Committee (HTCC) draft findings and decision on bronchial thermoplasty for asthma.

Timeline

Phase	Date	Public Comment Days
Technology recommendations published	January 5, 2016	
Public comments	January 5 to 20, 2015	**16**
Selected technologies published	February 4, 2016	
Public comments	February 4 to March 6, 2015	**31**
Draft key questions published	October 22, 2015	
Public comments	October 22 to November 4, 2015	**15**
Final key questions published	November 25, 2015	
Draft report published	February 16, 2016	
Public comments	February 7, to March 18, 2016	**30**
Final report published	April 8, 2016	
Public meeting	May 20, 2016	
Draft findings & decision published	June 7, 2016	
Public comments	June 8 to 21, 2016	**14**

Overview

Category	Comment Period *June 8 to 21, 2016*	Cited Evidence
Patient, relative, and citizen	0	0
Legislator and public official	0	0
Health care professional	3	0
Industry & manufacturer	1	1
Professional society & advocacy organization	0	0
Total	**4**	**1**

Comments

		Respondents		Cited Evidence
☐	1.	Amy Markevich, MD	Overlake Medical Center	N
☐	2.	Navdeep S. Rai, MD	Pulmonary Consultants	N
☐	3.	Maria B. Stewart, MD	Boston Scientific Corporation	Y
☐	4.	Michael Wechsler, MD	National Jewish Hospital	Y

[redacted]

From: Markezich, Amy <Amy.Markezich@overlakehospital.org>
Sent: Monday, June 20, 2016 4:12 PM
To: HCA ST Health Tech Assessment Prog
Subject: Bronchial Thermoplasty comments

I appreciate the opportunity I had to serve as the clinical expert for the committee discussion on bronchial thermoplasty (BT). I did want to bring up a few concerns I had about the decision and some of the discussion items.

I felt that the panel was operating on incomplete information about severe asthma, the procedure itself, and the impact on patient's lives. As a subject matter expert I was informed that my role was not to actively participate in the discussion, but only to answer questions when I was specifically asked. I would have appreciated the opportunity to clarify misunderstandings that came up about the disease process and burden of disease, as well as the known long term side effects of current therapy. If there was a pulmonologist on the committee, even as a non-voting member, who was allowed to freely participate in the discussion, I think the rest of the committee members would have had a much better understanding of the complex challenges we as specialists face in treating this very difficult subset of severe asthmatics, and the committee may have arrived at a different decision.

The patients who we consider for this procedure are the ones who we have completely maximized their medical therapy, and are still severely symptomatic on a daily basis, or have frequent hospitalizations. We do not consider patients for bronchial thermoplasty who only occasionally need to take prednisone to supplement a single controller inhaler. These are patients who are seen by asthma specialists, and are not only treated with inhaled corticosteroid therapy with long acting beta-agonist therapy, but also with leukotriene receptor antagonists and long acting anticholinergic therapy, and are still uncontrolled. Prior to consideration of bronchial thermoplasty, we also evaluate these patients for other treatments such as biologic therapies such as anti-IgE therapy (omalizumab) or anti-IL5 therapy (mepolizumab). The patients we consider for BT are ones that either don't meet the criteria for these biologic agents, or who have been on the biologic therapies for at least 6 months and have failed the therapy. Our patients continue to struggle from their severe disease and the long term effects of therapies. We often have to keep them on long term prednisone therapy, which is very well known to have a high risk of long term adverse effects. The lack of other therapeutic avenues forces physicians and patients to seek other alternative treatments such as chemotherapeutic agents like methotrexate or chronic antimicrobial therapies such as azithromycin. Despite the fact that these alternative therapies convey significant risk for side effects, patients and physicians must resort to these given the lack of access to other safer therapeutic modalities such as bronchial thermoplasty. I do not think the committee fully understood the severity of asthma for these patients, and in fact was even dismissive of that. Their symptoms and burden of disease are much more than being "scared by not being able to breathe". These are patients unable to go to the grocery store, unable to walk up stairs, unable to get through a day of work without the need for rescue inhalers. These patients have to miss work on an extremely frequent basis because they get hospitalized for asthma exacerbations, or they can't get through the work day because they have to be on a nebulizer 4-5 times a day. Many are unable to work at all because they have to miss so many work days.

As far as concerns over adverse effects of the procedure, the studies that have been done have shown a very low rate of adverse effects, most of them being an asthma exacerbation shortly after the procedure is done. I know the committee was concerned about the safety of the procedure, however what was not addressed was the known high risk of adverse effects of current standard therapy, in particular prednisone. Prednisone is well known to have high rates of severe adverse events, including diabetes, obesity, osteoporosis, avascular necrosis, cataracts, and glaucoma. We see patients get pathologic fractures all too often because of their steroid therapy. I have a patient who has already required bilateral hip replacements at the age of 32 because she developed avascular necrosis from prednisone. This is someone who is a candidate for bronchial thermoplasty, but whose insurance has denied the procedure. Instead, she has to deal with

complication after complication of her prednisone therapy. I think this consideration of the consequences of prednisone use would have helped the committee when they were discussing asthma therapies and the bronchial thermoplasty procedure.

When the committee discussed whether professional societies recommend this procedure in clinical practice, the committee looked at the recommendation of only one out of the three major US pulmonary and asthma societies. Both the American College of Chest Physicians (ACCP) and the American Academy of Allergy, Asthma & Immunology (AAAAI) recommend this procedure as an additional therapy for the treatment of severe asthma, and both societies have stated that there is enough evidence supporting the clinical use of the procedure that it should no longer be considered to be experimental. I strongly encourage the committee to take the recommendations of ACCP and AAAAI into consideration.

Lastly, one of the considerations the committee used to reach their decision was the discussion that patients who may be candidates for the procedure can always appeal to the HCA for compassionate use, or centers can still do the procedure through a research protocol, and can apply to the HCA to pay for the procedure through research. This is not a practical or realistic option. Most of the centers in Washington State that do this procedure are not set up to do clinical trials of this nature, and do not have the funding or the infrastructure to start these kinds of trials. I also argue that every single patient that I have requested insurance coverage for this procedure for qualifies for compassionate use, because we have already exhausted all of the currently available treatment options. Appealing for compassionate use on a case-by-case basis is a very burdensome process, and will result in patients being denied care that they need. Furthermore as the appeal process invariably drags on, patients suffer with both their disease and the consequences of treating such aggressive severe asthma. In addition, this decision affects more than just the patients covered through the HCA, as private insurance companies in this state will point to the HCA decision and use it as a reason to continue to deny coverage for the procedure (even though the same private carriers cover it in other states), so the argument that this decision only affects a very small group of patients is based on a flawed rationale.

Again, I appreciate the opportunity to participate in this process. I hope the committee considers this additional information, and I hope that the committee considers including subspecialists with expertise in the procedures being evaluated as more active panel members in the future.

Sincerely,
Amy Markezich, MD

Pulmonary Consultants P.L.L.C.

Pawan Chawla, M.D., P.S.
Ayesha Haroon, MD
Manuel G. Iregui, M.D., P.S.
Richard A. Kahlstrom, M.D., P.S.
Navdeep S. Rai, M.D., P.S.
Shinkai Hakimi, MD
Ramona Ionita, MD
Kurt Jensen, M.D., P.S.
Rajesh Kandasamy, MD
John T. Verrilli, M.D., P.S.

Washington State Health Care Authority

Health Technology Clinical Committee

June 17, 2016

Dear Members of the Committee,

I write to express my concern with the draft decision to not cover bronchial thermoplasty for the most needy of our state's patients. The decision runs counter to the recommendations of guidelines of Global Initiative for Asthma. This group was formed in 1993 with the support in the NIH's National Heart Lung and Blood Instuitue and World Health Organization. Its guidelines have been the standard for asthma management for more than two decades. Furthermore, the procedure has the endorsement of multiple medical societies, including American College of Chest Physicians, American College of Allergy, Asthma, and Immunology and British Thoracic Society as the standard of care for Severe Persistent Asthma failing medical management.

A medical procedure that is part of guidelines and endorsed by medical societies is considered Standard of Care and therefore can not be classified at Experimental or Investigational. Bronchial Thermoplasty should not be withheld from our state's population.

The draft's statement "All committee members found the effectiveness of the technology to be unproven" is inconsistent with the data and my own experience. I have treated 15 patients with this procedure. All of them have benefitted tremendously. They have stopped going to the emergency rooms with repeated flares, the usage of systemic steroids has dramatically been reduced, as have hospitalizations. In the meantime the patients who have not had the procedure continue to suffer daily dyspnea, frequent exacerbations and severe impairment of quality of life.

1708 Yakima, Suite 300 •Tacoma, Washington 98405 • Tel: (253) 572-5140 • Fax: (253) 272-0419
34509 9th Ave. S, #104 • Federal Way, Washington 98003 • Tel: 1 (877)572-1004 • Fax: (253) 722-5541
11511 Canterwood Blvd. NW, #300 • Gig Harbor, Washington 98332 • Tel: (253) 572-5140 • Fax (253) 851-2235

Pulmonary Consultants P.L.L.C.

Pawan Chawla, M.D., P.S.
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Manuel G. Iregui, M.D., P.S.
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The committee's draft finding " ....found safety to be less safe or unproven ..." is surprising. While a very small number of patients are hospitalized because of short term exacerbation, this is an expected result of stimulating a sensitive airway with a foreign body. The hospitalizations are no different than the need to hospitalize patients undergoing other invasive procedures. My 15 patients have had a total of 45 procedures as each patient requires 3 sessions to complete the full procedure. Of these 45 procedures, less than 5 have resulted in hospitalization.

The bottom line is that a medical procedure that is part of guidelines and endorsed by medical societies is considered Standard of Care and therefore no longer can be classified at Experimental or Investigational. The "complications" of asthma exacerbations immediately after the procedure are expected and short in duration. Bronchial Thermoplasty should not be withheld from our state's population. I urge you to reconsider your decision. I would be happy to discuss further with any and all on the committee.

Sincerely,

[redacted]

Navdeep S Rai, MD FACP FCCP

1708 Yakima, Suite 300 -Tacoma, Washington 98405 - Tel: (253) 572-5140 - Fax: (253) 272-0419
34509 9th Ave. S, #104 - Federal Way, Washington 98003 - Tel: 1 (877)572-1004 - Fax: (253) 722-5541
11511 Canterwood Blvd. NW, #300 - Gig Harbor, Washington 98332 - Tel: (253) 572-5140 - Fax (253) 851-2235

Corporate Headquarters
100 Boston Scientific Way
Marlborough, MA 01752

June 20, 2016

SUBMITTED ELECTRONICALLY

Josh Morse, MPH
Program Director
Washington State Healthcare Authority
Health Technology Assessment Program
P.O. Box 42712
Olympia, WA 98504-2712

Re: Comments on Washington State Health Care Authority (HCA) Final Evidence Report and Draft Decision on Bronchial Thermoplasty

Dear Mr. Morse:

Boston Scientific Corporation appreciates the opportunity to provide comments on the Final Evidence Report and Draft Decision on Bronchial Thermoplasty published by the Washington State Health Care Authority (HCA).

Bronchial thermoplasty is an innovative procedure for the treatment of severe persistent asthma in patients 18 years and older whose asthma is not well controlled with inhaled corticosteroids and long-acting beta2-agonists. Treatment with bronchial thermoplasty has been shown to significantly reduce healthcare utilization, presenting an opportunity to improve patient outcomes and quality of life while reducing overall health care costs. Bronchial thermoplasty has been shown to be a safe, effective, and long-lasting treatment option for a well-defined population of adults.

Boston Scientific was disappointed to see that many of our previously submitted comments and corrections to the Draft Evidence Report were not addressed in the Final Report and that the level of discussion at the May 20, 2016 meeting indicated a continued lack of understanding of (1) the definition of severe asthma; (2) the design of the clinical trials evaluating bronchial thermoplasty; and (3) Bayesian statistics, which are universally accepted as an appropriate statistical methodology in the right settings. Moreover, it was disappointing to see how the HCA Panel minimized the role of the one invited provider, Amy Markezich, MD (n.b. subject matter expert for the HCA Panel) who has direct experience with the technology and with treating poorly-controlled severe persistent asthma. Finally, we were dismayed to observe that the comments of providers of bronchial thermoplasty, along with those by treated patients who took time to travel and attend the meeting on May 20 were given very little consideration by the Panel.

Much of the Panel's commentary appeared to focus negatively on the role of industry in the development and study of bronchial thermoplasty. While we understand the inherent concerns of any technology assessment organization regarding the potential for bias in industry-sponsored research, we believe that the WA HCA approached the Final Evidence Report and the May 20 meeting with a pre-determined bias of its own that colored its ability to review the evidence objectively and give appropriate and fair consideration to bronchial thermoplasty as a therapeutic option for Washington state residents.

Additionally, in its conclusions after reaching a non-coverage decision, Panel members were heard to comment that providers could still access bronchial thermoplasty for patients in need by seeking exceptions to the non-coverage policy. These comments appear to diminish the important role of the Panel in providing Washington residents with access to medical technologies. They also demonstrate a lack of appreciation of the significant administrative burden that such exceptions represent, not only for providers, but also for the HCA itself, which would be forced to adjudicate each exception request at significant time and financial cost.

Having provided this feedback on the HCA's process, for the remainder of these comments we will focus on ongoing issues related to the interpretation and representation of the data on clinical outcomes and safety and the policy information associated with bronchial thermoplasty.

Specifically, our comments will address elements in the following categories:

1. Inaccuracies or Inappropriate Assessment of Clinical Trial Data/Outcomes in May 20 HCA Panel Presentations;
2. Definition of Severe Asthma;
3. Selection of Analytical Method (Bayesian Statistics);
4. Current Status of Guidelines, Commercial Insurance Coverage and Medicare Coverage for Bronchial Thermoplasty; and
5. Prior Comments Not Addressed in the Final Report (Appendix A).

Discussion

1. **Inaccuracies or Inappropriate Assessment of Clinical Trial Data/Outcomes in May 20 HCA Panel Presentations**
   In its presentations the HCA Panel often represented views that are not aligned with the conclusions to be drawn from the body of evidence on bronchial thermoplasty. Specifically:
   a. Quality of Life (QoL): As evidenced in slides 16/17 presented by Charisa Fotinos, Deputy Medical Director, bronchial thermoplasty has demonstrated non-worsening changes in ACQ and AQLQ within RCTs. Specifically, there is no decrease in QoL and suggestive evidence of a potential improvement in QoL (as evidenced in the AIR and RISA meta-analysis results). These results appear to answer Key Question #1 re: "Clinical Effectiveness…" and are aligned with outcomes of interest to the HCA Panel. These positive results were not summarized alongside potential concerns within the Agency Medical Director Summary, and this omission could introduce selection bias.

b. Asthma Control: Across the studies of bronchial thermoplasty (slide 19), there was not an observed change in rescue medication use. However, the Asthma Control Questionnaire (ACQ) showed, similar to QoL, no decrease in control and evidence that may be considered suggestive of improved control (meta-analysis of AIR/RISA results; slide 16). These results appear to answer Key Question #1 re: "Clinical Effectiveness…" and are aligned with outcomes of interest to the HCA Panel. These positive results were not summarized alongside potential concerns within the Agency Medical Director Summary, and this omission could also introduce selection bias.

c. Exacerbations: Within the most rigorous trial to date – AIR2 – reductions in exacerbations have been demonstrated (both controlled and using the bronchial thermoplasty-recipients as their own control). The Panel completely failed to understand the study design for the AIR2 Trial where 2-week periods of medication withdrawal were used to evaluate the impact of bronchial thermoplasty on exacerbations. Moreover, within the earlier AIR study, a significant reduction of exacerbations was also observed among those randomized to bronchial thermoplasty, above and beyond that observed within the control group. As noted in the study:

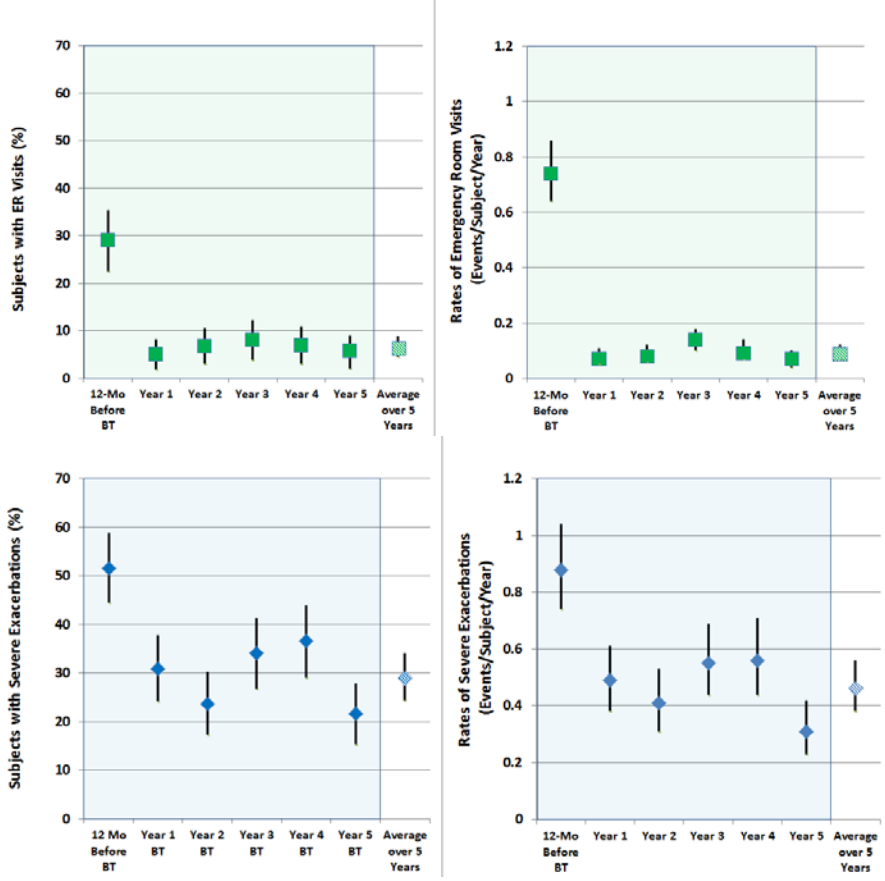
"Twelve months after the last study treatment, the mean number of mild exacerbations in the bronchial-thermoplasty group was 0.18±0.31 per subject per week, as compared with 0.35±0.32 at baseline. The number of mild exacerbations in the control group was 0.31±0.46 per subject per week, as compared with 0.28±0.31 at baseline. The difference between the two groups in the change from baseline was significant at 3 months and at 12 months (P = 0.03 for both comparisons) but not at 6 months (Fig. 2). As compared with baseline, the average number of exacerbations during the 2-week periods at 3, 6, and 12 months when subjects in the two groups were treated with inhaled corticosteroids alone was reduced in the bronchial-thermoplasty group but was not significantly changed in the control group (−0.16±0.37 vs. 0.04±0.29 per subject per week, P = 0.005 for the comparison between the groups). Analysis with the use of the Wilcoxon rank-sum method also showed a significant difference between the groups (P = 0.01). This finding can be extrapolated to approximately 10 fewer mild exacerbations per subject per year in the bronchial-thermoplasty group".[1]

d. Lung Function: Unlike bronchodilators or corticosteroids that increase airway caliber and thereby increase FEV_1, bronchial thermoplasty does not affect FEV_1 values because its mechanism of action is to attenuate the hyper-reactivity of airways by impacting airway smooth muscle (ASM) during an asthma exacerbation. Considering the procedure's mechanism of action, it is therefore apparent that FEV_1 is not an appropriate measure of effectiveness. FEV_1 does, however, remain an important measure of safety. Data from multiple trials of bronchial thermoplasty have demonstrated no deterioration

[1] Cox G, *et al*. Asthma Control during the Year after Bronchial Thermoplasty. *N Engl J Med* 2007;356:1327-37.

in FEV_1 over time, confirming no negative impact on airway caliber (i.e., strictures or narrowing) in the long term.

e. Reduced Hospitalizations & Emergency Department (ED) Visits: As presented during Dr. Michael Wechsler's testimony, ED visits and exacerbations (linked to hospitalizations) were durably reduced during the 5-years of follow up. (Figures in Dr. Wechsler's slides #6 and #7 are depicted below). The Panel completely discarded the publication on the durability of bronchial thermoplasty because they appeared not to understand or appreciate the concept of a non-inferiority clinical trial and instead used their commentary to criticize the editors of a leading peer-review journal for publishing clinical trial data generated from such a study design.



f. Safety:

<u>Adverse Events</u>

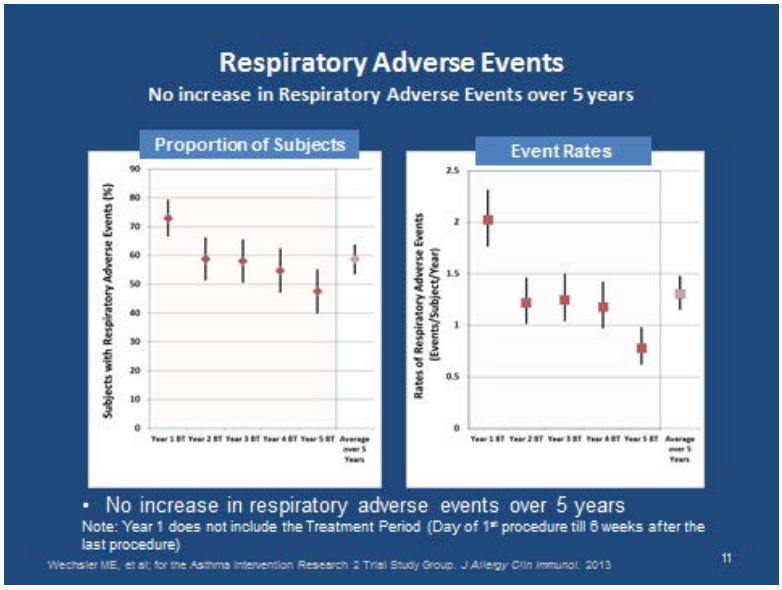
There is an increase in peri-procedural complications (including in a small fraction of treated patients, potential hospital admissions) associated with bronchial thermoplasty. However, the WA HCA failed to note the context associated with the adverse events, which was provided in each peer-reviewed publication for each RCT:

As noted within the AIR2 trial[2]: *"The majority of respiratory adverse events occurred within 1 day of the bronchoscopy and resolved within 7 days…All these events resolved with standard therapy"*

As noted within the AIR trial[3]:
"In the bronchial thermoplasty group, the majority of the adverse events occurred within 1 day after the procedure and resolved an average of 7 days after the onset of the event."

As noted within the RISA trial[4]:
"After bronchial thermoplasty, there was an increase in respiratory adverse events in the treatment period, but there was no increase in the frequency of adverse events with successive treatments. There was no difference between groups during the post-treatment period. The most frequently observed respiratory adverse events in the treatment period for bronchial thermoplasty subjects were wheezing, cough, chest discomfort, dyspnea, productive cough, and discolored sputum. Most of these adverse events occurred within 1 day of the bronchoscopy procedure and resolved on average within a week."

Moreover, during the post-treatment period, there was no observed increase in the rate of hospitalizations or adverse events in bronchial thermoplasty-treated patients.[5]



[2] Castro M, *et al*. Effectiveness and Safety of Bronchial Thermoplasty in the Treatment of Severe Asthma: A Multicenter, Randomized, Double-Blind, Sham-Controlled Clinical Trial. *Am J Respir Crit Care Med* Vol 181. pp 116–124, 2010.
[3] Cox G, *et al*. Asthma Control during the Year after Bronchial Thermoplasty. *N Engl J Med* 2007;356:1327-37.
[4] Pavord ID, *et al*. Safety and Efficacy of Bronchial Thermoplasty in Symptomatic, Severe Asthma. *Am J Respir Crit Care Med* Vol 176. pp 1185–1191, 2007.
[5] Torrego, S.A. Munoz, AM, *et al*. Bronchial thermoplasty for moderate or severe persistent asthma in adults. *Cochrane Database of Systematic Reviews* 2014. Issue 3. Art. No.: CD 009910.

Bronchiectasis

Within slide 20, Charisa Fotinos, Deputy Chief Medical Officer notes that "Increase incidence of bronchiectasis in Castro F/U of 2%, (usually reported per 100,000 person years)."

While the rate of 2% is accurate as reported by high-resolution CT (~2/98 patients), the comparison provided is inappropriate, as this rate "usually reported per 100,000" is for the general population rather than for the severe asthma population.[6] Additionally, these rates are specific to the United Kingdom rather than the United States population.

When considering a severe asthma population, the rate of bronchiectasis has been reported to range from 4%-20%.[7,8]

Boston Scientific respectfully requests the Final Findings and Decision documentation be amended to note both that the appropriate comparison of the rate of bronchiectasis to be ~4%-20%, and that the rate observed within the "Castro F/U" may be suggestive of a protective effect of bronchial thermoplasty.

Competing Risks

Finally with regards to safety, Boston Scientific asks that the WA HCA Panel consider the idea of competing risks in the assessment of bronchial thermoplasty for severe, difficult-to-treat asthmatics with few, if any, remaining treatment options. While the Panel is right to try to assess and manage the risks associated with technologies under their review (including bronchial thermoplasty), it should be acknowledged that there is a risk in doing nothing as well. Notably, this risk may be an order of magnitude greater than the risk associated with bronchial thermoplasty. In a 2008 paper, a mortality rate of 6.7 per 100 person-years was observed among severe, poorly-controlled asthmatics. This compares to approximately (conservatively, assuming all 4,000 commercially treated patients were treated in the prior 12 months) approximately 3 in 4,000 person years (approximately 0.075 per 100 person years).[9]

These two statistics taken together are suggestive of a potential protective effect of bronchial thermoplasty. One potential mechanism of action for this protective effect would be a reduction in asthma exacerbations.

g. Cost Effectiveness: The HCA Panel is incorrect in its assertion that bronchial thermoplasty is not cost-effective. Three peer-reviewed, published cost-

[6] Quint JK *et al*. Thoraz 2012.

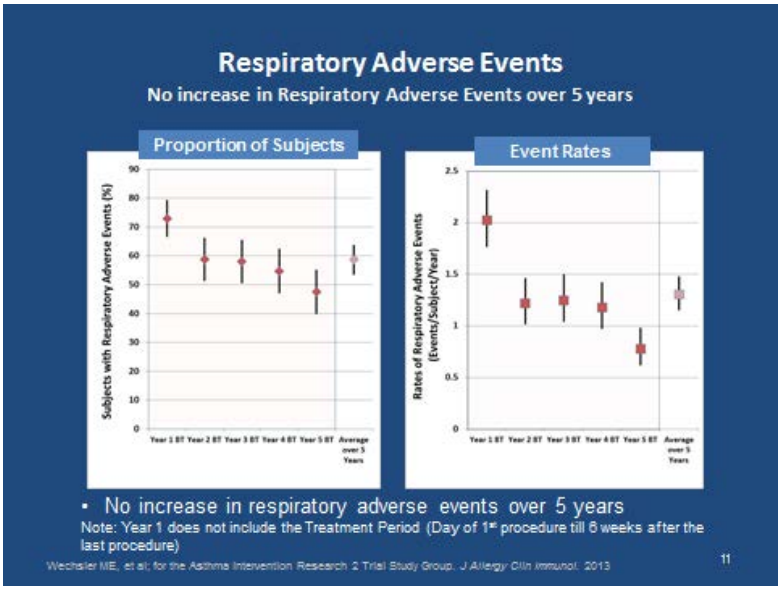
[7] 4% - Lujan *et al*. Prevalence of Bronchiectasis in Asthma according to Oral Steroid Requirement: Influence of Immunoglobulin Levels. *BioMed Research International* 2013.

[8] 20% - Bilton D and Jones AL. Bronchiectasis: Epidemiology and Causes. *Eur Respir Mon* 2011. (52) 1-10.

[9] Omachi et al. 2008; Ann Allergy Asthma Immunol. 2008 Aug; 101(2):130-136.

effectiveness analyses have consistently quantified benefits that echo the conclusions of the Hayes Final Evidence Report: bronchial thermoplasty produces significant gains in quality of life in the short term, and over the longer-term generates economic savings in the form of avoided exacerbations and healthcare resource utilization. Importantly, all three publications found that bronchial thermoplasty is cost-effective.[10,11,12] Even if the HCA Panel dismisses the cost-effectiveness analysis conducted with Boston Scientific's involvement (Cangelosi, *et al)*, which would be inappropriate given that the publication was subject to the same rigorous peer-review process as the non-industry analyses, there are two additional independent publications that both reach the same conclusion: bronchial thermoplasty is cost-effective.

h. Inconsistency between Conclusions and Decision: The decision of the WA HCA Panel appears to diverge from conclusions of Hayes, Inc., the independent, third-party consultancy engaged to conduct the assessment. In its presentation, Hayes concluded that, "Overall, evidence suggests that bronchial thermoplasty may provide some benefits in the short term and does not pose major safety concerns [in the short term]." Results from the AIR2 Extension study support this conclusion for the long-term, as there was no demonstrated increase in adverse events.



[10] Zein *et al*. Cost effectiveness of bronchial thermoplasty in patients with severe uncontrolled asthma. *J Asthma*. 2016 Mar;53(2):194-200. doi: 10.3109/02770903.2015.1072552. Epub 2015 Sep 17.

[11] Zafari *et al*. Cost-Effectiveness of Bronchial Thermoplasty, Omalizumab, and Standard Therapy for Moderate-to-Severe Allergic Asthma. *PLoS One*. 2016 Jan 11;11(1):e0146003. doi: 10.1371/journal.pone.0146003. eCollection 2016.

[12] Cangelosi *et al*. Cost-effectiveness of bronchial thermoplasty in commercially-insured patients with poorly controlled, severe, persistent asthma. *Expert Rev Pharmacoecon Outcomes Res*. 2015 Apr;15(2):357-64. doi: 10.1586/14737167.2015.978292. Epub 2014 Nov 1.

Boston Scientific respectfully requests that the WA HCA correct the each of the described inaccuracies and biases associated with its assessment of bronchial thermoplasty.

2. Definition of Severe Asthma

At the May 20 public meeting, the HCA Panel members repeatedly stated that they did not consider patients evaluated in the AIR2 Trial as having severe asthma because their FEV_1 values were around 70% of predicted. Dr. Amy Markezich, the invited expert in pulmonology, explained that FEV_1 alone does not define asthma severity. She clearly stated that she does not consider FEV_1 alone when assessing the severity of a patient's asthma and that the level of symptoms and medication levels must also be considered. The reviewer from Hayes also made the Panel aware that the Castro 2010 publication noted that in the AIR2 trial 86% of the bronchial thermoplasty subjects and 88% of the sham group subjects met the American Thoracic Society criteria for severe refractory asthma. Despite this information and the expert pulmonologist's input, the Panel spent an inordinate amount of time focusing on FEV_1 as an indicator of severity and concluding that patients in AIR2 were not severe asthmatics.

Boston Scientific asks that the HCA consider the definition of severe asthma as stated in the ATS-ERS guidelines (2013):

"Any one of the following four criteria qualifies a patient as having uncontrolled asthma: 1) Poor symptom control: ACQ consistently >1.5 or ACT <20 (or "not well controlled" by NAEPP or GINA guidelines over the 3 months or evaluation); 2) Frequent severe exacerbations: 2 or more bursts of systemic CSs (>3 days each) in the previous year; 3) Serious exacerbations: at least one hospitalization, Intensive Care Unit stay or mechanical ventilation in the previous year; and 4) Airflow limitation: FEV1<80% predicted (in the presence of reduced FEV_1/FVC defined as less than the normal lower limit) following a withhold of both short- and long-acting bronchodilators.

Evidence for any one of these four criteria while on current high-dose therapy identifies the patient as having "severe asthma". Patients who do not meet criteria for uncontrolled asthma, but whose asthma worsens on tapering of corticosteroids, will also meet the definition of severe asthma. Fulfilment of this definition predicts a high degree of future risk both from the disease itself (exacerbations and loss of lung function), as well as from side-effects of the medications."[13]

During the discussion, the WA HCA Panel argued that the patients treated in AIR2 did not have severe asthma because the FEV_1 average in the trial was 78% of predicted. Based on the ATS-ERS guideline's definition of severe asthma, an average FEV_1 of 78% of predicted alone would identify this patient population as having severe asthma. However, even patients among the study population who may

[13] Chung KF, Wenzel SE, *et al*. 6. International ERS/ATS Guidelines on Definition, Evaluation and Treatment of Severe Asthma. 2013.

have had FEV_1 levels ≥80% predicted were severe asthmatics based on the presence of poor symptom control and frequent severe exacerbations, which were both among the inclusion criteria for AIR2.

Boston Scientific therefore respectfully requests that the WA HCA clarify its position on the AIR2 patient population to acknowledge that this group had severe persistent asthma.

3. **Selection of Analytical Method (Bayesian Statistics)**

During the May 20 meeting, the HCA Panel was critical of the use of Bayesian statistics to assess both effectiveness and safety in AIR2. Moreover, the representative from Hayes, Inc. who prepared and provided a detailed review of published clinical evidence acknowledged a lack of knowledge and expertise in assessing data analyzed using Bayesian statistics. The absence of an expert statistician on the HCA Panel to provide an informed opinion to guide the discussion clearly undermined the consideration of the data and once again highlights a flawed process. Boston Scientific is concerned that the Panel's apparent bias against Bayesian statistics, stemming from a total lack of understanding of statistical techniques and its failure to consult with an appropriate expert, resulted in an incomplete/unfair assessment of bronchial thermoplasty.

The importance of Bayesian statistics in clinical trials has been well established. In this regard, the FDA employs a large number of Bayesian statisticians to carefully review clinical trials that use Bayesian statistics and has developed a Guidance Document that addresses the use of Bayesian statistics in clinical trials.[14] The guidance document states that the FDA must advocate for taking the least burdensome approach to approval of a product. Specifically, it states that, "The Bayesian approach, when correctly employed, may be less burdensome than a frequentist approach.1 Section 513(a)(3) of the Federal Food, Drug, and Cosmetic Act (FFDCA) mandates that FDA shall consider the least burdensome appropriate means of evaluating effectiveness of a device that would have a reasonable likelihood of resulting in approval (see 21 U.S.C. 360c(a)(3))."[15]

During the May 20 meeting, the HCA Panel argued that the Castro 2010 publication did not provide any prior distributions that could have informed the Bayesian design and therefore the use of Bayesian statistics was inappropriate. In actuality, it is not correct that no priors were used. Informative priors from both the AIR and RISA studies were used but not described in detail due to the need to meet word limitations commonly associated with manuscript publication.

Even if informative priors from AIR and RISA had not been used, the Panel's

[14] Center for Biologics Evaluation and Research and Center for Devices and Radiological Health. U.S. Department of Health and Human Services. Food and Drug Administration. Division of Biostatistics. Office of Surveillance and Biometrics. Guidance for Industry and FDA Staff: Guidance for the Use of Bayesian Statistics in Medical Device Clinical Trials. Document issued on: February 5, 2010.

[15] Ibid.

criticism of the use of non-informative prior distributions is inappropriate and confirms a lack of understanding of Bayesian statistics. According to the FDA Guidance Document, "The Bayesian approach is also frequently useful in the absence of prior information. First, the approach can accommodate adaptive trials (e.g., interim analyses, change to sample size, or change to randomization scheme) and even some unplanned, but necessary trial modifications."[16] Furthermore, "Non-informative prior distributions are used frequently in Bayesian adaptive trials when no prior information is available. As another example, in a Bayesian hierarchical model for combining studies, a non-informative prior distribution may be placed on a parameter that captures the variability between studies because, ordinarily, no informative prior is available on this parameter."[17]

Boston Scientific cautions the HCA Panel that to discount a pivotal piece of evidence (AIR2) on the basis of a lack of understanding of the analytic method, when the same analytic method was deemed by the FDA to be sufficient to evaluate safety and efficacy, may introduce significant unwanted bias into the coverage process.

Boston Scientific respectfully requests that the Washington HCA seek input from a proven expert in Bayesian analyses to inform its coverage recommendation. Non-coverage of a technology because of an incomplete/improper assessment of the related data without the involvement of the right subject matter experts should not be a reason to deny patients access to breakthrough therapeutic options.

4. **Current Status of Guidelines, Commercial Insurance Coverage and Medicare Coverage for Bronchial Thermoplasty**

Despite Boston Scientific's prior clarification of the status of guidelines, statements of support and insurance coverage for bronchial thermoplasty, the WA HCA Panel declined to update its Final Report or its presentations on May 20. If the HCA Panel is going to consider the lack of coverage in its assessment of bronchial thermoplasty or any other therapy, it must also consider existing coverage if its final decision is to be objective. Important guidelines, statements of support from professional specialty societies or recognized asthma authorities, and positive coverage policies were not included in the HCA Panel's review.

Boston Scientific again requests that the following guidelines, statements of support insurance coverage policies, and publications be considered, and that the HCA amend its decision to be more reflective of existing coverage for bronchial thermoplasty by providing for coverage with conditions.

a. The INTERASMA manifesto on bronchial thermoplasty (http://www.interasma.org/images/manifesto3.pdf);

[16] Ibid.
[17] Ibid.

b. The statement on bronchial thermoplasty by the American College of Allergy, Asthma, and Immunology (http://college.acaai.org/publications/advocacy-insider/statement-bronchial-thermoplasty); and

c. The Diagnosis and Management of Asthma –Pediatric/Adult – Inpatient/Ambulatory Clinical Practice Guideline, developed by a task force of representatives from the University of Wisconsin (UW) Medical Foundation, UW Hospital and Clinics, UW Health Department of Family Medicine and Internal Medicine, Unity Health Insurance, Physicians Plus Insurance Corporation, and Group Health Cooperative (2015)(Attached as Appendix B).

d. Recently, a review article by Trivedi *et al*. recommended bronchial thermoplasty for specific patients, stating "in patients with severe uncontrolled asthma on inhaled corticosteroids plus a second controller with a predominant chronic airflow obstruction component (with or without reversibility of lung function to normal with bronchodilator treatment) or patients who do not respond to or are not candidates for anti-IgE or anti-interleukin 5, bronchial thermoplasty is a treatment option."[18]

e. Although the HCA is correct that some commercial insurers have published non-coverage policies for bronchial thermoplasty, there are several large insurers that do cover the procedure (please refer to Appendix C). These positive coverage policies should be considered to assure factual accuracy and non-biased assessment.

Within slide 21, the HCA Panel notes the absence of a National Coverage Decision (NCD) for bronchial thermoplasty, suggesting that this absence represents CMS's non-coverage of bronchial thermoplasty. Although the HCA Panel is correct that Medicare does not have an NCD for bronchial thermoplasty, it is not appropriate to interpret the absence of an NCD as proof of non-coverage. CMS has noted that NCDs "… are reserved for interventions deemed particularly controversial or expected to have a significant impact on the Medicare program."[19]

Thus, the absence of a National Coverage Decision can be more appropriately interpreted as evidence that CMS has simply deemed bronchial thermoplasty not to have a significant impact on the Medicare program. Moreover, CMS previously approved a Transitional Pass-Through Payment for the Alair™ Catheter used in bronchial thermoplasty procedures, which required the agency to determine that the procedure offered substantial clinical improvement.

Finally, Medicare does provide implicit coverage of the procedure when medically necessary, as it falls within a covered benefit category and there is no documented

[18] Trivedi A, Pavord I and Castro M. Bronchial thermoplasty and biological therapy as targeted treatments for severe uncontrolled asthma. www.thelancet.com/respiratory. Published online May 23, 2016. http://dx.doi.org/10.1016/S2213-2600(16)30018-2.

[19] Centers for Medicare and Medicaid Services. Medicare Program; revised process for making Medicare national coverage determinations. *Federal Register*. 2003; 68(187):55634–41.

non-coverage at either the local or national level.

We ask that the HCA correct its representation of Medicare coverage to allow for more objective assessment of the current coverage landscape.

Summary and Closing

To summarize our comments, Boston Scientific notes that the May 20 review of bronchial thermoplasty by the HCA Panel was flawed as a process. We strongly request that the HCA immediately address the various issues discussed in the body of this letter and reverse its recommendation of noncoverage of bronchial thermoplasty to instead provide for coverage with conditions. We believe that a fair and unbiased review of the evidence would likely have resulted in a recommendation of coverage with conditions for bronchial thermoplasty. A revised decision will provide access to residents of Washington State with severe persistent asthma that is poorly controlled with inhaled corticosteroids and long-acting beta2-agonists who may be appropriate candidates for the procedure.

Please do not hesitate to contact me should you have any questions or need clarification.

Sincerely,

Maria B. Stewart
Director, Health Economics & Reimbursement, Endoscopy Division

Appendix A: Prior Comments Not Addressed in Final Report

In Boston Scientific's comments to the Draft Evidence Report, we addressed several concerns and inaccuracies. Specifically, we were concerned about the following issues:

a. Studies Considered in the FDA Review Process: repeated statements that the FDA approval was based on a single, double-blind sham-controlled RCT (AIR2) do not take into account that the FDA also considered the consistency of AIR2 findings with prior RCTs (AIR and RISA).
b. Interpretation and Representation of Clinical Trial Data: while we will discuss issues of interpretation and representation of trial data at the May 20 meeting separately, we were concerned to note that in the Final Report, the following concerns were not referenced or addressed:
    i. Misrepresentation of the prevalence of asthma attacks, inaccurately conveyed the difference in improvement in AQLQ between subjects in the treatment group versus subjects in the control group of AIR2
    ii. Hypothesizing without supportive evidence that there is a loss of benefits from bronchial thermoplasty during longer follow-up
    iii. Dismissal of statistically significant clinically meaningful changes in secondary outcomes
    iv. Misinterpretation of hospital costs associated with bronchial thermoplasty
    v. Misstatement of statistics produced using the Bayesian analytical method
    vi. Citation of data related to off-label uses of bronchial thermoplasty
    vii. Selective citation of outcomes from the RISA trial, leaving out important improvements in patient outcomes and patient satisfaction;
    viii. Statement that bronchial thermoplasty is not cost-effective despite referencing three peer-reviewed published assessments concluding that the procedure is cost-effective;
    ix. Omission of mention that the statistical significance of the decrease in the incidence of respiratory and adverse events from years 1 to 5 was ($P<0.00001$); and
    x. Inflammatory statements regarding the bias of industry-sponsored research.
c. Use of the GRADE Methodology to Assess the Quality of Bronchial Thermoplasty Evidence: the HCA did not consider evidence that the GRADE methodology has only limited ability to discriminate between estimates that will remain stable in the future and those that will change and also to associate respective likelihoods of stability within an expected outcome, as described by Gartlhner, *et al*..[20]
d. Current Status of Guidelines, Statements of Support and Insurance Coverage Policies: In its final report, the HCA continued to only reference non-coverage while not mentioning any of the existing coverage policies for bronchial thermoplasty. The HCA also failed to update the Final Report to reflect numerous guidelines and statements of support for bronchial thermoplasty omitted from the Draft Report.

[20] Gartlehner e. al., The predictive validity of quality of evidence grades for the stability of effect estimates was low: a meta-epidemiological study. Journal of Clinical Epidemiology 70 (2016) 52-60.

Appendix B: Unity Health Insurance Guideline for the Diagnosis and Management of Asthma

Guideline for the Diagnosis and Management of Asthma in Adult and Pediatric Patients

The Clinical Practice Guideline for the Diagnosis and Management of asthma in Adult and Pediatric Patients was reviewed and approved by Unity's Clinical Quality Improvement Committee (CQIC) on September 25, 2015. The guideline was previously approved by CQIC on November 15, 2013, September 16, 2011, November 20, 2009; November 16, 2007; November 18, 2005; November 19, 2004; November 14, 2002; January 8, 2001; and February 3, 1999. The UW Medical Foundation, UW Hospital and Clinics, UW Health Department of Family Medicine and Internal Medicine, Unity Health Insurance, Physicians Plus Insurance Corporation, and Group Health Cooperative participated in the development and revision of this guideline. The task force was a multidisciplinary work group comprised of physicians, asthma specialists, a pharmacist, nurses, and quality improvement staff.

Diagnosis and Management of Asthma – Pediatric/Adult – Inpatient/Ambulatory Clinical Practice Guideline

Table of Contents

Note: Active Table of Contents -- Click to follow link

Release Date: July 2015

Expiration Date: July 2017

Executive Summary

Guideline Overview

We agreed to endorse the 2015 Global Initiative for Asthma (GINA) *Global Strategy for Asthma Management and Prevention Guideline* (accessed 5/15/15).[1]

Key Practice Recommendations & Companion Documents

We supports the following key recommendations summarized from GINA[1], in addition to those recommendations found within the 2015 GINA quick-reference pocket guides available online (accessed on 5/15/15):

- GINA Pocket Guide for Asthma Management and Prevention (Age 6 or older)
- GINA Pocket Guide for Asthma Management and Prevention (Age 5 or younger)

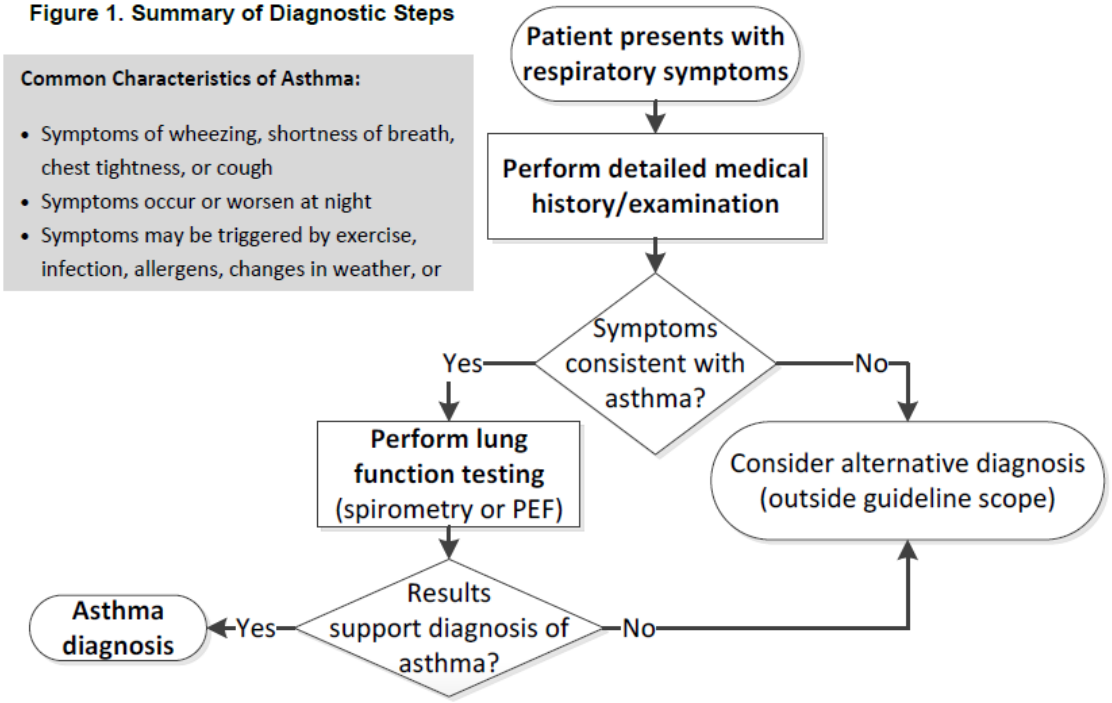
WHAT IS ASTHMA?

Asthma is a chronic inflammatory disorder of the airways which causes symptoms of wheezing, shortness of breath, tightness in the chest, and cough that may vary in frequency and over time.

ESTABLISHING A DIAGNOSIS

It is recommended to complete a medical history to establish respiratory symptoms, as well as lung function testing using spirometry or peak expiratory flow (PEF) (see **Figure 1**). A diagnosis of asthma may be made after consideration of a patient's history and whether the patient exhibits variable expiratory airflow limitations (i.e., difficulty exhaling due to bronchoconstriction, airway wall thickening, and increased mucus).

Figure 1. Summary of Diagnostic Steps

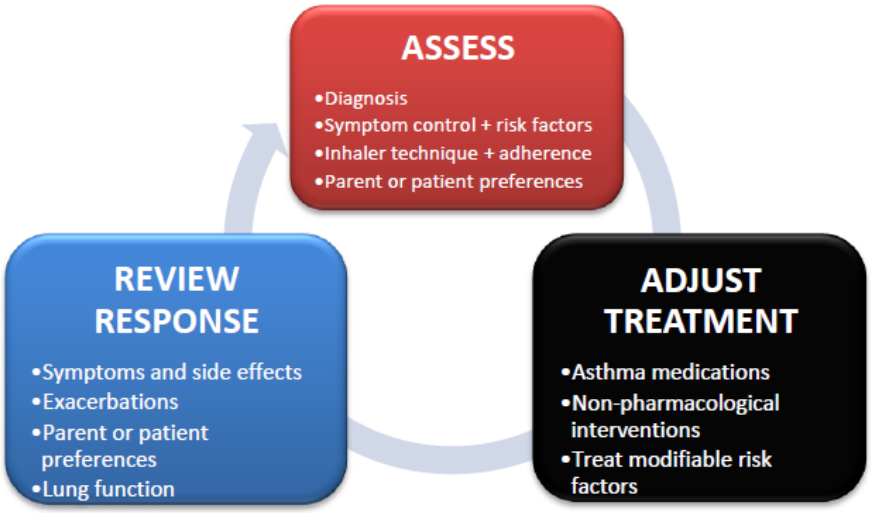


PROVIDING TREATMENT AND ASSESSMENT

The goals of asthma treatment include:

- Prevention of chronic asthma symptoms and asthma exacerbations;
- Maintenance of normal activity levels;
- Patient satisfaction with asthma care and quality of life (i.e., having normal or near normal lung function, experiencing no or minimal side effects).

Asthma treatment should follow a repeating pattern of assessment of control, adjustment of treatment, and review of response to the treatment.



Assessment

An age-appropriate questionnaire should be used to help determine asthma control and efficacy of the treatment plan. It is recommended to assess asthma control at least annually.

- Asthma Control Test (ACT) for patients age 12 years or older.
- Childhood Asthma Control Test (cACT) for patients age 6-11 years.
- Test for Respiratory and Asthma Control in Kids (TRACK) for patients age 5 years or younger.

Treatment

The age-differentiated Stepwise Approach to Control should be used to guide the prescription of asthma medication (controllers and rescue). A full listing of medications available in the United States is summarized in the Asthma Rescue and Controller Medication Table, and dosing options for inhaled corticosteroids are available in the Asthma Medication Dosing Table.

All patients should have a written asthma action plan, which should include:

- A list of medications and a description of how to use them
- Environmental triggers

Patients age 18 years or older with uncontrolled severe-persistent asthma, despite use of recommended therapeutic regimens and referral to an asthma specialist (Step 5) may be candidates for a non-pharmacological intervention of Bronchial Thermoplasty.

Review Response
It is recommended that patients be seen every 1-3 months after initiating treatment and every 3-12 months thereafter.

Patients should be seen by the provider managing their asthma within 1 week following an exacerbation to re-evaluate the patient compliance and treatment plan efficacy.

MANAGING ASTHMA EXACERBATIONS
Asthma exacerbations are acute or subacute episodes of progressively worsening asthma symptoms (i.e., shortness of breath, coughing, wheezing, chest tightness).

Treatment algorithms should be followed to guide exacerbation management within the outpatient, emergency department, and inpatient settings:

- Asthma Exacerbation- Primary Care Algorithm

- Asthma Exacerbation- Emergency Department (Pediatric) Algorithm
- Asthma Exacerbation- Inpatient (Pediatric) Algorithm

- Asthma Exacerbation- Emergency Department (Adult) Algorithm
- Asthma Exacerbation- Inpatient (Adult) Algorithm

Companion Documents

1. GINA Pocket Guide for Asthma Management and Prevention (Age 6 or older)
2. GINA Pocket Guide for Asthma Management and Prevention (Age 5 or younger)
3. GINA Appendices to the Global Strategy for Asthma Management and Prevention

Patient Resources

1. Health Information: Asthma
2. Health Information: Asthma Action Plan
3. Health Information: Asthma Action Plan: Green Zone
4. Health Information: Asthma Action Plan: Yellow Zone
5. Health Information: Asthma Action Plan: Red Zone
6. Health Information: Asthma and GERD
7. Health Information: Asthma and Vocal Cord Problems
8. Health Information: Asthma and Wheezing
9. Health Information: Asthma Attack
10. Health Information: Asthma Diary
11. Health Information: Asthma During Pregnancy
12. Health Information: Asthma in Children
13. Health Information: Asthma in Children: Helping a Child Use A Metered-Dose Inhaler and Mask Spacer
14. Health Information: Asthma in Children: Knowing How Bad an Attack Is

Scope

Disease/Condition(s): Asthma

Clinical Specialty: Pulmonary, Allergy, Family Medicine, Internal Medicine, Pediatrics, Hospitalists, Respiratory Therapy, Emergency Medicine

Intended Users: Physicians, Advanced Practice Providers, Respiratory Therapists, Registered Nurses, Pharmacists, Asthma Educators

CPG objective(s): To provide evidence-based recommendations for the management of asthma across age groups and clinical settings.

Target Population: Any pediatric (0-11 years), adolescent (12-17 years), or adult (18 years or older) patient diagnosed with asthma.

Methodology

The GINA guideline[1] was produced using the standard methodology of the GINA Science Committee outlined on page vi of the full guideline (http://www.ginasthma.org).

Rating Scheme for the Strength of the Evidence/Recommendations:

Sources of evidence		Definition
A	Randomized controlled trials (RCTs) and meta-analyses. Rich body of data.	Evidence is from endpoints of well designed RCTs or meta-analyses that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of patients.
B	Randomized controlled trials (RCTs) and meta-analyses. Limited body of data.	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.
C	Nonrandomized trials. Observational studies.	Evidence is from outcomes of uncontrolled or non-randomized trials or from observational studies.
D	Panel consensus judgement.	This category is used only in cases where the provision of some guidance was deemed valuable but the clinical literature addressing the subject was insufficient to justify placement in one of the other categories. The Panel Consensus is based on clinical experience or knowledge that does not meet the above listed criteria.

Introduction

Asthma is a chronic inflammatory disorder of the airways. In susceptible individuals, this inflammation causes recurrent episodes of coughing (particularly at night or early in the morning), wheezing, breathlessness, and chest tightness. These episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment. The goals of asthma therapy are to prevent chronic asthma symptoms and asthma exacerbations, maintain normal activity levels, have normal or near normal lung function, experience no or minimal side effects and have patient satisfaction with asthma care.

Recommendations

We endorse the recommendations outlined within the 2015 GINA Guideline[1] located online at http://www.ginasthma.org/documents/4 (accessed on 5/15/15).

The full guideline document references appendices, located here: http://www.ginasthma.org/local/uploads/files/GINA_Appendix_2015.pdf (accessed on 5/18/15).

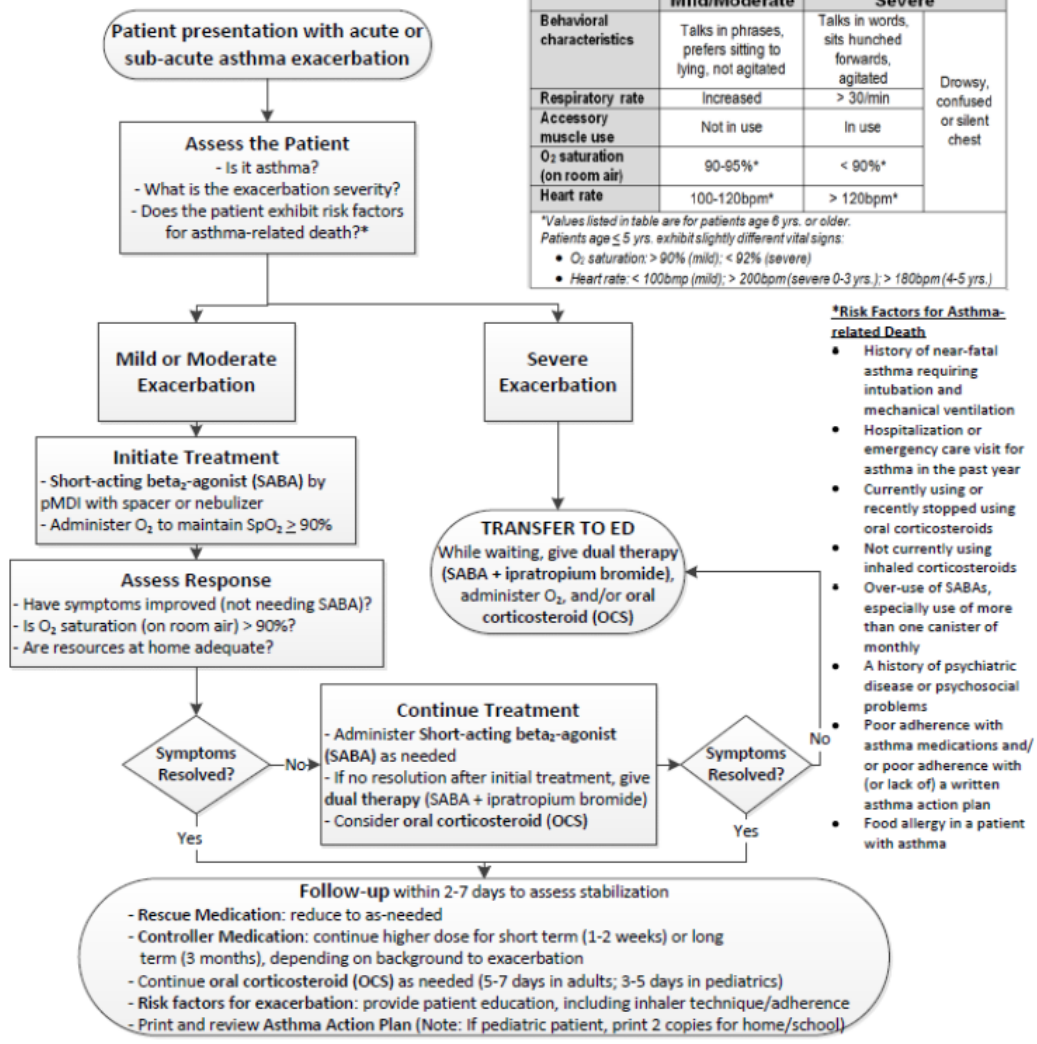
Disclaimer

CPGs are described to assist clinicians by providing a framework for the evaluation and treatment of patients. This Clinical Practice Guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

References

1. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2015. Available from www.ginasthma.org
2. Gorelick MH, Stevens MW, Schultz TR, Scribano PV. Performance of a Novel Clinical Score, the Pediatric Asthma Severity Score (PASS), in the Evaluation of Acute Asthma. *Academic Emergency Medicine*. 2004;11(1):10-18.

Management of Asthma Exacerbation in Primary Care (Age 2 years or older)



Determine Exacerbation Severity	Mild/Moderate	Severe	
Behavioral characteristics	Talks in phrases, prefers sitting to lying, not agitated	Talks in words, sits hunched forwards, agitated	Drowsy, confused or silent chest
Respiratory rate	Increased	> 30/min	
Accessory muscle use	Not in use	In use	
O_2 saturation (on room air)	90-95%*	< 90%*	
Heart rate	100-120bpm*	> 120bpm*	

*Values listed in table are for patients age 6 yrs. or older.
Patients age ≤ 5 yrs. exhibit slightly different vital signs:
- O_2 saturation: > 90% (mild); < 92% (severe)
- Heart rate: < 100bmp (mild); > 200bpm (severe 0-3 yrs.); > 180bpm (4-5 yrs.)

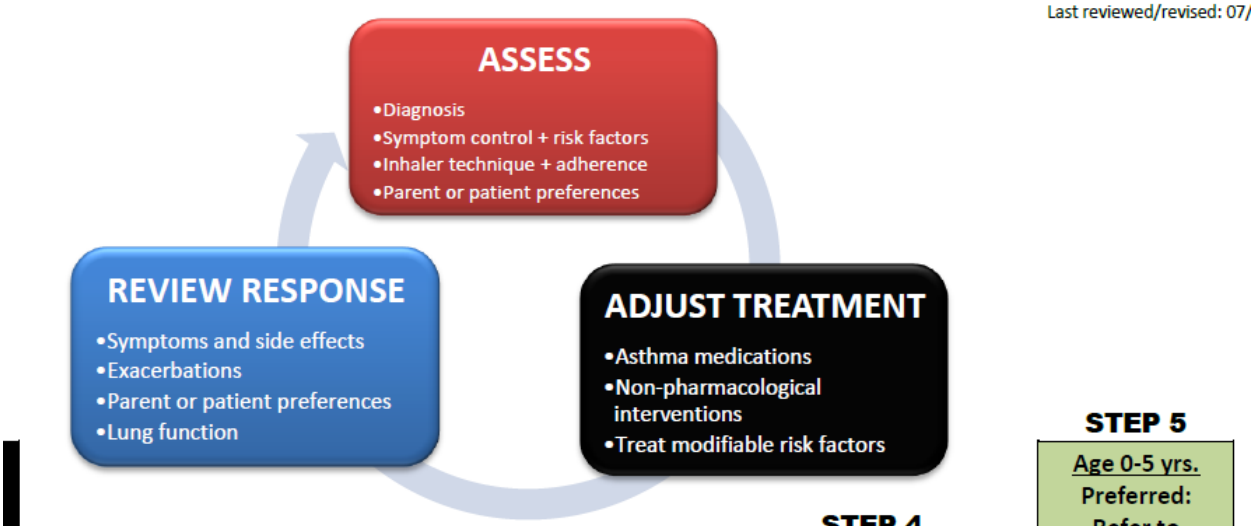
***Risk Factors for Asthma-related Death**

- History of near-fatal asthma requiring intubation and mechanical ventilation
- Hospitalization or emergency care visit for asthma in the past year
- Currently using or recently stopped using oral corticosteroids
- Not currently using inhaled corticosteroids
- Over-use of SABAs, especially use of more than one canister of monthly
- A history of psychiatric disease or psychosocial problems
- Poor adherence with asthma medications and/or poor adherence with (or lack of) a written asthma action plan
- Food allergy in a patient with asthma

Medications		Dose & Frequency	Route
Short-acting Beta2-agonist (SABA)	albuterol	(age < 12 yrs.) 2.5 mg Q20min x3 (age ≥ 12 yrs.) 5 mg Q20min x3	Nebulizer
		4-8 puffs Q20min x3	pMDI + spacer
Ipratropium	ipratropium bromide	(age < 5 yrs.) 250 mcg Q20min x3 (age ≥ 5 yrs.) 500 mcg Q20min x3	Nebulizer
Oral Corticosteroid (OCS)	methylprednisolone (age < 12 yrs.)	1-2 mg/kg in 2 divided doses; max 60 mg per day	Oral
	prednisone (age ≥ 12 yrs.)	1 mg/kg/day PO in 1-2 divided doses; max 50 mg/day	Oral
Corticosteroid Alternative	*dexamethasone (age ≤ 18 yrs. only)*	*0.6 mg/kg per dose 36-48 hrs. apart; max 16 mg/dose*	*Oral*

Stepwise Approach to Asthma Symptom Control

Last reviewed/revised: 07/



STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
All Ages *Alternative:* *Low dose ICS*	**Age 0-5 yrs.** **Preferred:** **Low dose ICS** *Alternatives:* *LTRA or intermittent ICS*	**Age 0-5 yrs.** **Preferred:** **Double low dose ICS** *Alternative:* *Add LTRA*	**Age 0-5 yrs.** **Preferred:** **Refer to asthma specialist** *Alternatives:* *Add LTRA or increase ICS frequency or add intermittent ICS*	**Age 0-5 yrs.** **Preferred:** **Refer to asthma specialist**
	Age 6-11 yrs. **Preferred:** **Low dose ICS** *Alternatives:* *LTRA*	**Age 6-11 yrs.** **Preferred:** **Medium dose ICS or Low dose ICS + LABA** *Alternative:* *Low dose ICS + LTRA*	**Age 6-11 yrs.** **Preferred:** **Refer to asthma specialist** *Alternatives:* *Medium dose ICS + LABA or High dose ICS + LABA*	**Age 6-11 yrs.** **Preferred:** **Refer to asthma specialist** *Alternative:* *Omalizumab*
	Age ≥ 12 yrs. **Preferred:** **Low dose ICS** *Alternatives:* *LTRA or theophyline*	**Age ≥ 12 yrs.** **Preferred:** **Low dose ICS + LABA** *Alternatives:* *Medium dose ICS or Low dose ICS + LTRA + theophyline*	**Age ≥ 12 yrs.** **Preferred:** **Medium dose ICS + LABA** *Alternatives:* *High dose ICS + LABA and/or LTRA + theophylline or add tiotropium**	**Age ≥ 12 yrs.** **Preferred:** **Refer to asthma specialist** *Alternatives:* *Add tiotropium*or omalizumab or bronchial thermoplasty**

**For adult patients only. Not indicated or recommended for patients younger than 18 years.*

All Ages

Preferred: PRN Short-acting Beta$_2$-agonist (SABA)

Consider stepping up if uncontrolled symptoms, exacerbations or risks. Always evaluate diagnosis, inhaler technique, and adherence before making therapy changes.

Consider stepping down if symptoms controlled for 3 months and low risk for exacerbations.

Ceasing ICS is not advised

10

Table 1. Asthma Medications Chart

NOTE: The following table objectively outlines selected asthma medications available in the United States, and does not provide recommendations for or against their use. The listing does not indicate inclusion on the formulary. Prescribing providers should refer to specific formulary listings for status of various agents.

	Medication	Inhaler	Nebulization Solution	Oral (Injectable products where noted)	Purpose	Considerations
RESCUE Medications	***Short-acting beta agonists***					
	Albuterol Sulfate - ProAir® MDI - Proventil® MDI - Ventolin® MDI - Accuneb® nebulization - VoSpire® ERT	108 mcg/act	0.63 mg/3 mL 1.25 mg/3 mL 2.5 mg/3 mL 5 mg/mL	Tablet: 2 mg, 4 mg Oral Syrup: 2 mg/5 mL ERT: 4 mg, 8 mg	Bronchodilation through smooth muscle relaxation	Although available, oral albuterol is not recommended.
	Levalbuterol - Xopenex® MDI - Xopenex® nebulization	45 mcg/act	0.31 mg/3 mL 0.63 mg/3 mL 1.25 mg/3 mL 1.25 mg/0.5 mL			
	Terbutaline - tablet - injection			Tablet: 2.5 mg, 5 mg Injection: 1 mg/mL		
	Short-acting anticholinergics					
	Ipratropium Bromide - Atrovent® MDI - Atrovent ® nebulization	17 mcg/act	0.5 mg/2.5 mL		Bronchodilation through inhibition of muscarinic receptors to reduce intrinsic vagal tone of the airway	May be an alternative to short-acting beta agonists in patients who cannot tolerate short-acting beta agonists
	Combination short-acting beta agonist and short-acting anticholinergic					
	Albuterol Sulfate/Ipratropium Bromide - Combivent Respimat® MDI - Duoneb® nebulization	100/20 mcg/act	2.5/0.5 mg/3 mL		See individual agents	
	Systemic corticosteroids					
	Prednisone - tablet - Rayos® delayed-release tablet - solution - Intensol® concentrated solution			Tablet: 1 mg, 2.5 mg, 5 mg, 10 mg, 20 mg, 50 mg Delayed-release tablet: 1 mg, 2 mg, 5 mg Solution: 5 mg/5 mL 5 mg/1 mL		
	Methylprednisolone - Medrol® tablet - Solu-Medrol® injection			Tablet: 2 mg, 4 mg, 8 mg, 16 mg, 32 mg Pak: 4 mg tablets x 21 Injection: 40 mg, 125 mg, 500 mg, 1000 mg		
	Dexamethasone - Tablet - Solution - Intensol® concentrated solution - Elixir			Tablet: 0.5 mg, 0.75 mg, 1 mg, 1.5 mg, 2 mg, 4 mg, 6 mg Solution: 0.5 mg/5 mL 1 mg/mL Elixir: 0.5 mg/5 mL Injection: 4 mg/mL, 10 mg/mL		

MDI: metered dose inhaler
DPI: dry powder inhaler
ERT: extended-release tablet
inh: inhalation
act: actuation

	Medication	Inhaler	Nebulization Solution	Oral (Injectable products where noted)	Purpose	Considerations
CONTROLLER Medications	***Long-acting beta agonists***					
	Formoterol Fumarate - Foradil Aerolizer® DPI - Perforomist® nebulization	12 mcg/inh	20 mcg/2 mL		Bronchodilation	Should be used in combination with an inhaled corticosteroid
	Salmeterol Xinafoate - Serevent Diskus ® DPI	50 mcg/inh				
	Inhaled corticosteroids					
	Beclomethasone Dipropionate - Qvar® MDI	40 mcg/act 80 mcg/act			Reduce airway hyperrespon-siveness, inhibit inflammatory cell migration and activation, and block late phase reaction to allergen	MDIs may be used with a spacer
	Budesonide - Pulmicort Flexhaler® DPI - Pulmicort® nebulization	90 mcg/inh 180 mcg/inh	0.25 mg/2 mL 0.5 mg/2 mL 1 mg/2 mL			
	Ciclesonide - Alvesco® MDI	80 mcg/act 160 mcg/act				
	Flunisolide - Aerospan® MDI	80 mcg/act				
	Fluticasone Furoate - Arnuity Ellipta® MDI	100 mcg/act 200 mcg/act				
	Fluticasone Propionate - Flovent Diskus® DPI - Flovent® MDI	DPI: 50 mcg/inh 100 mcg/inh 250 mcg/inh MDI: 44 mcg/act 110 mcg/act 220 mcg/act				
	Mometasone Furoate - Asmanex® DPI - Asmanex® MDI	DPI: 110 mcg/inh 220 mcg/inh MDI: 100 mcg/act 200 mcg/act				
	Combination long-acting beta agonists and corticosteroid					
	Budesonide/Formoterol Fumarate - Symbicort® MDI	80/4.5 mcg/act 160/4.5 mcg/act			See individual agents	
	Mometasone Furoate /Formoterol Fumarate - Dulera® MDI	100/5 mcg/act 200/5 mcg/act				
	Fluticasone Propionate/ Salmeterol Xinafoate - Advair Diskus® DPI - Advair® MDI	DPI: 100/50 mcg/inh 250/50 mcg/inh 500/20 mcg/inh MDI: 45/21 mcg/act 115/21 mcg/act 230/21 mcg/act				
	Long-acting anticholinergics					
	Tiotropium - Spiriva® Handihaler DPI - Spiriva® Respimat MDI	DPI: 18 mcg/inh MDI: 2.5 mcg/act			Bronchodilation through inhibition of muscarinic receptors to reduce intrinsic	

					vagal tone of the airway	
	Mast cell stabilizers					
	Cromolyn -nebulization		20 mg/2 mL		Stabilize mast cells	
	Methylxanthines					
	Aminophylline - injection			Injection: 25 mg/mL	Bronchodilation through smooth muscle relaxation and the suppression of airway response to stimuli	
	Theophylline Theochron® 12-hour ERT - 24-hour ERT - Theo-24® 24-hour ER capsule - oral solution - Elixophyllin® elixir - injection			12-hour ERT: 100 mg, 200 mg, 300 mg, 450 mg 24-hour ERT: 400 mg, 600 mg 24-hour ER capsule: 100 mg, 200 mg, 300 mg, 400 mg Solution and Elixir: 80 mg/15 mL Injection: 0.8 mg/mL, 1.6 mg/mL		
CONTROLLER Medications	***Leukotriene Modifiers***					
	Montelukast - Singulair®			Tablet: 10 mg Chewable tablet: 4 mg, 5 mg Packet: 4 mg	Interfere with the pathway of leukotriene mediators, which are released from mast cells, eosinophils, and basophils.	
	Zafirlukast - Accolate®			Tablet: 10 mg, 20 mg		
	Zileuton - Zyflo® - Zyflo ER®			Tablet: 600 mg 12-hour ERT: 600 mg		
	Immunomodulators					
	Omalizumab - Xolair®			Injection: 150 mg vial	Prevents binding of IgE to the high-affinity receptors on basophils and mast cells	

MDI: metered dose inhaler
DPI: dry powder inhaler
ERT: extended-release tablet
inh: inhalation
act: actuation

Asthma Medications- Low, Medium and High Doses of Inhaled Corticosteroids

This table provides an estimate of comparative daily doses for inhaled corticosteroids administered to children and adults with asthma. It may be used in conjunction with the Stepwise Approach to Asthma Symptom Control found within the Asthma Guideline.

Medication	Daily Dose (mcg)								
	Low			Medium			High		
	Child (≤ 5 yrs.)	Child (6-11 yrs.)	Adult (≥ 12 yrs.)	Child (≤ 5 yrs.)	Child (6-11 yrs.)	Adult (≥ 12 yrs.)	Child (≤ 5 yrs.)	Child (6-11 yrs.)	Adult (≥ 12 yrs.)
Beclomethasone HFA	100	50-100	80-240	NA	>100-200	>240-480	NA	>200	>480
Budesonide DPI	200	100-200	180-540	NA	>200-400	>540-1080	NA	>400	>1080
Budesonide (nebule)	250-500	250-500	NA	>500-1000	>500-1000	NA	>1000	>1000	NA
Ciclesonide HFA	160	80	80-160	NA	>80-160	160-320	NA	>160	>320
Flunisolide HFA	NA	160	320	NA	320	>320-640	NA	>640	>640
Fluticasone HFA	100	100-200	44-264	>100-352	>200-500	>264-440	>352	>500	>440
Fluticasone DPI	NA	100-200	100-300	NA	>200-400	>300-500	NA	>400	>500
Momentasone DPI	NA	110	110-220	NA	≥220-<440	220-440	NA	≥440	>440

Last reviewed/revised: 07/2015

References:

1. Global Intiative for Asthma. Global Strategy for Asthma Management and Prevention, 2015. Available from www.ginasthma.org
2. Program NAEAP. Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma-Summary Report 2007. *J Allergy Clin Immunol*. 2007; 120(5 Suppl):S94-138.

Corticosteroids- Administration & Dosage. *Facts & Comparisons eAnswers* 2015; http://online.factsandcomparisons.com/MonoDisp.aspx?fromtables=fandc-hcp14409&monoid=fandc-hcp10549. Accessed July 1, 2015

Bronchial Thermoplasty Summary for Primary Care Providers

Overview: Bronchial Thermoplasty (BT) is an innovative procedure for the treatment of severe persistent asthma. This procedure is performed in an outpatient setting under moderate sedation, and is accomplished in three separate bronchoscopic sessions scheduled approximately 3 weeks apart. In the first procedure, airways under direct vision and reachable by the bronchoscope in the right lower lobe are treated. During the second procedure, targeted airways in the left lower lobe are treated, and in the third and final procedure, targeted airways in both upper lobes are treated.[1-2]

Target Population: A potential treatment option for highly-selected patients aged 18 years and older with uncontrolled asthma, despite use of recommended therapeutic regimens and referral to an asthma specialist (Step 5).[3] *(GINA Evidence B)*

Outcomes: Bronchial thermoplasty has been studied in four clinical studies in patients with asthma; three of which were randomized controlled clinical trials and the results for which have been published in peer-reviewed journals. Most notably, published data from the Asthma Intervention Research 2 (AIR2) clinical trial demonstrates that bronchial thermoplasty continues to show benefits in adult patients with severe uncontrolled asthma out to at least five years.[4] Bronchial thermoplasty was shown to provide long term asthma control, demonstrated by a sustained reduction in the rate of severe exacerbations (asthma attacks) and emergency room (ER) visits over a five year period after treatment.[5]

Risk assessment: The most common side effect found in the clinical studies was an expected transient increase in the frequency and worsening of respiratory-related symptoms, including asthma (multiple symptoms), respiratory tract infections, wheezing, dyspnea, and chest pain.
Long-term follow-up out to 5 years has been completed in 4 studies: the safety profile for the BT treated patients has demonstrated consistency over time based on the percent of subjects reporting respiratory adverse events, the number of respiratory adverse events per subject, and the number of hospitalizations and emergency room visits due to respiratory symptoms per subject.

Pre-Approval Needs: While non-coverage policies exist, there is a need to request pre-approval to the insurer by submitting documentation that supports a severe asthma diagnosis. This documentation is inclusive of differentiating other respiratory-related disorders (i.e., COPD, bronchiectasis, vocal cord dysfunction, obstructive sleep apnea), management of comorbidities (i.e., allergic rhinitis, sinusitis, GERD), and observations of compliance and/or attempts to manage their asthma with current standard medications (i.e., minimum of ICS+LABA) over at least a 3 month period yet still demonstrating evidence of exacerbations, activity limitation and/or risk of future exacerbations. As coverage policies get implemented, a shorter, more specific pre-authorization form may be required.

Last reviewed/revised: 07/2015

References:
1. Cox G, Miller JD, McWilliams A, Fitzgerald JM, Lam S. Bronchial thermoplasty for asthma. Am J Respir Crit Care Med. 2006;173(9):965-969.
2. ECRI. Bronchial Thermoplasty for Treating Adult Patients with Severe Persistent Asthma. 2013.
3.Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2015. Available from: www.ginasthma.org
4. Castro M, Rubin AS, Laviolette M, et al. Effectiveness and safety of bronchial thermoplasty in the treatment of severe asthma: a multicenter, randomized, double-blind, sham-controlled clinical trial. Am J Respir Crit Care Med. 2010;181(2):116-124.
5. Wechsler ME, Laviolette M, Rubin AS, et al. Bronchial thermoplasty: Long-term safety and effectiveness in patients with severe persistent asthma. J Allergy Clin Immunol. 2013;132(6):1295-1302.e1293.

Appendix C: Commercial Payers Covering BRONCHIAL THERMOPLASTY as of June 20, 2016

Health Plan	State/Region	Approximate Number of Covered Lives	Policy Link
Avera Health Plans	IA, NE, SD	70,000	
AvMed	FL	300,000	
CareFirst BlueCross BlueShield	MD, VA, DC	3,400,000	Medical Policy (No. 7.01.102
Health Care Service Corporation (HCSC) Operating through BlueCross BlueShield plans in Illinois, Montana, New Mexico, Oklahoma and Texas	IL, MT, NM, OK, TX	14,500,000	Medical Policy (SUR706.014)
HealthChoice	OK	217,000	
HealthPartners	MN	700,000	Medical Policy (No. 53678)
Independence Health Group: including Independence Blue Cross, AmeriHealth, AmeriHealth Administrators, and AmeriHealth Caritas	AL, CA, DC, DE, FL, GA, IL, IN, KY, LA, MD, MI, MN, MO, NC, NE, NJ, NY, NV, OK, PA, RI, SC, TN, TX, WV, VA	2,500,000	Medical Policy
Ohio State University Health Plan	OH	58,000	
Optima Health	VA	444,000	
PreferredOne	MN	350,000	Medical Criteri (No. MC/K002
Priority Health	MI	600,000	Medical Policy (No. 91577-R0

Health Plan	State/Region	Approximate Number of Covered Lives	Policy Link
SelectHealth	ID, UT	634,000	
Tufts Health Plan	MA, RI	1,033,640	Medical Policy
Unity Health	WI	90,000	Asthma CPG
University of Cincinnati Health	OH	10,000	
TOTAL		**24,906,640**	

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Michael Wechsler, MD MMSc
Professor of Medicine
Director of Asthma
Co-Director, NJH Cohen Family Asthma Institute
Department of Medicine
Direct Line: 303-398-1085
Cell Phone: 617-285-4987
Fax: 303-398-1780
Email: WechslerM@NJHealth.org

June 20, 2016

Josh Morse, MPH
Program Director
Washington State Healthcare Authority
Health Technology Assessment Program
P.O. Box 42712
Olympia, WA 98504-2712

Dear Mr. Morse:

I am writing to provide comments on the Washington State Health Care Authority's (HCA) final evidence report and draft decision on bronchial thermoplasty. I am a clinical specialist in pulmonary medicine and a researcher in severe asthma, and I have extensive experience performing bronchial thermoplasty in both research and clinical settings. I attended the May 20, 2016 Public Meeting and was disappointed in the process and the resulting non-coverage recommendation made despite the body of evidence and testimony supporting a role for BT in managing severe asthma. I wish to comment on some of the clinical discussions and assumptions associated with the HCA's assessment and the panel's recommendation not to cover bronchial thermoplasty but rather to leave access to the technology up to clinicians' ability to appeal.

During the meeting, there was significant discussion about the AIR2 patient population's severity of asthma, bias due to industry sponsorship, the strength of the clinical trial evidence, safety, generalizability of results, and patient selection. I was surprised when panel members spent significant time discussing FEV_1 as a measure of severity of asthma and asserting that because AIR2 had an average FEV_1 of 78% predicted results are not generalizable to the severe asthma patient population. While it is a factor, FEV_1 alone does not define a severe asthma patient. The American Thoracic Society (ATS) – European Respiratory Society (ERS) guidelines state that in addition to airflow limitation (defined by FEV_1), symptom control, exacerbations requiring steroid bursts, validated questionnaires, and medications needed for symptom control like inhaled corticosteroids, long-acting beta agonists and other controller medications including oral corticosteroids, are also important considerations for determination of asthma severity and control.[1] Notably, the ATS-ERS

[1] From: Chung KF et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. Eur Respir J 2014; 43: 343–373 | DOI: 10.1183/09031936.00202013
Table 3: Definition of Severe Asthma
Asthma which requires treatment with guidelines suggested medications for GINA steps 4–5 asthma (high dose ICS# and LABA or leukotriene modifier/theophylline) for the previous year or systemic CS for o50% of the previous year to prevent it from becoming ''uncontrolled'' or which remains ''uncontrolled'' despite this therapy Uncontrolled asthma defined as ***at least one*** (emphasis added) *of the following:*
1) Poor symptom control: ACQ consistently >.1.5, ACT <20 (or ''not well controlled'' by NAEPP/GINA guidelines)

guidelines do mention FEV_1 <80% predicted as one criterion indicating severe asthma, however the average FEV_1 of patients in AIR2 falls within the ATS-ERS defined parameter. During the May 20 discussion, the panel did not seem to take this into consideration when discussing the AIR2 trial patient population, which was defined in collaboration with asthma experts and, more importantly, with the FDA, to study BT in a severe asthma population.

During the meeting, there was also significant concern expressed about bias, as the principal studies of bronchial thermoplasty were sponsored by the manufacturer of the device used in the procedure. I understand the concern regarding bias, but as a researcher participating in numerous pharmaceutical and device trials, I question the fairness of disregarding the strict level of oversight and input provided by the FDA on the design of AIR2 and other bronchial thermoplasty trials as well as the rigorous review of the procedure and related data by a panel of experts prior to regulatory approval. If the HTA is to limit coverage to only those procedures or medications whose data are generated without industry involvement, it will be severely restricting patients' ability to access innovative therapies, and nearly every currently covered drug or device-related procedure in the State of Washington and elsewhere would need to be re-examined given the prevalence of industry sponsorship.

As an investigator in the AIR2 trial, the pivotal trial most heavily considered by the FDA in its PMA review and panel discussion, I am uniquely familiar with the trial data associated with bronchial thermoplasty. While it is correct that there was a placebo effect noted in the sham group, it is important to remember that for the outcomes of greatest importance to patients and in actual practice, such as emergency department visits, severe exacerbations, and days missed from work and school, bronchial thermoplasty was significantly more effective than sham. Specifically, bronchial thermoplasty reduced severe exacerbations by 32%, emergency room visits by 84%, and days missed from work and school by 66% versus sham. These are real outcomes that represent significant improvements in patients' quality of life and significant savings for the health care system, and these clinical benefits were shown to be durable over at least five years.

I was disappointed that the panel seemed to discount the impact of the 5 year data which has led to BT being included in several guidelines around the globe including the Global Initiative of Asthma, the British Thoracic Society, the American College of Chest Physicians, and others. Discounting these important 5-year data may inappropriately place Washington State residents in a position of inappropriate, inequitable access to technologies demonstrated to be not only effective, but durably safe. I would strongly urge the panel to consider all available evidence – including in particular the 5-year follow-up data – describing the patient experience when treated with BT to produce an informed and equitable decision; selectively disregarding pieces of evidence may inappropriately introduce bias to the panel's decision.

I was also disappointed by the panel's vote on bronchial thermoplasty safety data. Procedure related adverse events do occasionally occur, however in practice, as in the trials, they are typically managed with standard therapy, are predictable in timing (per-procedural within ~3 days)[2] and, are more than offset by the reductions in exacerbations demonstrated over a 5 year period. This observation of an offset reduction in exacerbations outweighing these peri-procedural risks was noted by the California

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2) Frequent severe exacerbations: two or more bursts of systemic CS (>3 days each) in the previous year
3) Serious exacerbations: at least one hospitalisation, ICU stay or mechanical ventilation in the previous year
4) Airflow limitation: after appropriate bronchodilator withhold FEV1 ***<80% predicted*** (emphasis added) *(in the face of reduced FEV1/FVC defined as less than the lower limit of normal); (note: 78%<80%)*
5)Controlled asthma that worsens on tapering of these high doses of ICS or systemic CS (or additional biologics)

[2] Castro, 2010. Effectiveness and safety of bronchial thermoplasty in the treatment of severe asthma: a multicenter, randomized, double-blind, sham-controlled clinical trial. Am J Respir Crit Care Med. 2010 Jan 15;181(2):116-24. doi: 10.1164/rccm.200903-0354OC. Epub 2009 Oct 8.

Technology Assessment Forum, which noted that BT "improves net health outcomes".[3] In addition, the long-term 5-year safety data from all three RCTs are consistent, well understood and acceptable. In my opinion, BT is a safe procedure with a well-characterized long-term safety profile.

Importantly, the outcomes seen in AIR2 are directionally consistent with those seen in prior randomized controlled trials - AIR and RISA - and the results are also consistent with my own post-approval clinical experience. In my practice, I have treated over 25 patients with bronchial thermoplasty and have noted significant improvement in symptoms and exacerbations in almost all of my patients with minimal and easily manageable side effects.

I was surprised to note that the panel seemed to disregard three available cost-effectiveness analyses because AIR2 data were included. The published cost-effectiveness data have leveraged the available published clinical data describing the efficacy of BT – including, but not limited to AIR2 and also including AIR and RISA studies. These studies have quantified and echoed the conclusions of the Hayes Final Evidence Report: BT produces significant gains in quality of life in the short term, and over the longer-term generates economic savings in the form of avoided exacerbations and healthcare utilization. Importantly, all three publications concluded that BT is cost-effective.[4,5,6]

Finally, I would also like to address patient selection. As a clinician treating many patients with poorly controlled severe asthma, I would not recommend bronchial thermoplasty for every patient. Rather, I would suggest that the criteria discussed in peer-reviewed literature and guidelines, as well as in other coverage policies, provide excellent benchmarks for Washington HCA to use in providing access to the therapy. Specifically, in a recent review article by Trivedi *et al*. published in *The Lancet*, the authors state that,

> *" [for] patients with severe uncontrolled asthma on inhaled corticosteroids plus a second controller with a predominant chronic airflow obstruction component (with or without reversibility of lung function to normal with bronchodilator treatment) or patients who do not respond to or are not candidates for anti-IgE or anti-interleukin 5, bronchial thermoplasty is a treatment option."*[7]

This phenotype represents a select group of patients for whom the only other treatment option - oral corticosteroids - produces significant negative side effects and causes deleterious comorbidities and reductions in quality of life. Moreover, the patient population described by Trivedi *et al*. is substantially similar in nature to the patient populations described by currently available coverage policies around the country. Although the panel spent time discussing which insurers are *not* covering bronchial thermoplasty, there was no acknowledgement of the numerous major payers throughout the country that *are* covering the procedure.

Currently., nearly all of the bronchial thermoplasty coverage policies require preauthorization, which is appropriate and could be considered by Washington HCA for bronchial thermoplasty (i.e., coverage

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[3] Tice JA. California Technology Assessment Forum: Bronchial Thermoplasty for the Treatment of Severe Asthma. October 19, 2011.

[4] Zein et al. Cost effectiveness of bronchial thermoplasty in patients with severe uncontrolled asthma. J Asthma. 2016 Mar;53(2):194-200. doi: 10.3109/02770903.2015.1072552. Epub 2015 Sep 17.

[5] Zafari et al. Cost-Effectiveness of Bronchial Thermoplasty, Omalizumab, and Standard Therapy for Moderate-to-Severe Allergic Asthma. PLoS One. 2016 Jan 11;11(1):e0146003. doi: 10.1371/journal.pone.0146003. eCollection 2016.

[6] Cangelosi et al. Cost-effectiveness of bronchial thermoplasty in commercially-insured patients with poorly controlled, severe, persistent asthma. Expert Rev Pharmacoecon Outcomes Res. 2015 Apr;15(2):357-64. doi: 10.1586/14737167.2015.978292. Epub 2014 Nov 1.

[7] Trivedi A, Pavord I and Castro M. Bronchial thermoplasty and biological therapy as targeted treatments for severe uncontrolled asthma. www.thelancet.com/respiratory. Published online May 23, 2016. http://dx.doi.org/10.1016/S2213-2600(16)30018-2,

with conditions). During the May 20 meeting, panel members mentioned that even non-covered therapies may be accessed if a provider appeals to WA HCA for an exception to the policy. While this may be true, this position abdicates authority of the HCA process to the treating clinician and access to BT could be determined by treating clinicians' ability to navigate this process rather than patients' true and objectively defined clinical need. The current recommendation of non-coverage with the option to request exceptions will likely result in patients who are well-qualified for and in need of bronchial thermoplasty continuing to experience severe exacerbations and/or develop the negative side effects and comorbidities associated with oral steroids. Most practicing clinicians do not have the administrative resources to support case-by-case appeals of non-coverage decisions. A preauthorization process with detailed eligibility criteria congruent with the GINA guidelines would eliminate the need for physicians whose patients need the therapy to take on the more taxing administrative burden of appealing to Washington HCA on a case-by-case basis and provide appropriately evaluated and vetted patients with reliable but well-governed access to the procedure. Having an established positive coverage policy with conditions would also ensure greater consistency in terms of which patients gain access to bronchial thermoplasty, as an exception process can be substantially more subjective in nature, leaving Washington HCA open to concerns about equal patient access.

Thank you for your consideration of these comments. I urge the HCA to reconsider its non-coverage decision and provide coverage with conditions so that appropriate patients in Washington State can access bronchial thermoplasty.

Sincerely,

Michael Wechsler, MD, MMSc
Professor of Medicine at National Jewish Health
Director of the Asthma Program
Co-Director of The Cohen Family Asthma Institute

Washington State Health Care Authority
Health Technology Assessment

Health Technology Clinical Committee
Findings and Decision

Topic: Bronchial Thermoplasty for Asthma
Meeting Date: May 20, 2016
Final Adoption:

Meeting materials and transcript are available on the HTA website:
www.hca.wa.gov/hta/meetingmaterials/Forms/ExtMeetingMaterials.aspx

Number and Coverage Topic:
20160520A – Bronchial Thermoplasty for Asthma

HTCC Coverage Determination:
Bronchial thermoplasty for asthma is **not a covered benefit.**

HTCC Reimbursement Determination:

Limitations of Coverage: NA

Non-Covered Indicators: NA

Agency Contact Information:

Agency	Phone Number
Labor and Industries	1-800-547-8367
Public Employees Health Plan	1-800-200-1004
Washington State Medicaid	1-800-562-3022

HTCC Coverage Vote and Formal Action:

Committee Decision

Based on the deliberations of key health outcomes, the committee decided that it had the most complete information: a comprehensive and current evidence report, public comments, and state agency utilization information. The committee concluded that the current evidence on bronchial thermoplasty for asthma is sufficient to make a determination on this topic. The committee discussed and voted on the evidence for use of bronchial thermoplasty for asthma compared to current alternative strategies. The committee considered the evidence and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

Based on these findings, the committee voted to not cover bronchial thermoplasty for asthma.

	Not Covered	Covered Under Certain Conditions	Covered Unconditionally
Bronchial Thermoplasty For Asthma	7	4	0

Discussion

The committee reviewed and discussed the available studies of bronchial thermoplasty. Details of study design, inclusion criteria and other factors affecting study quality were discussed. All committee members found the effectiveness of the technology to be unproven and a majority found safety to be less safe or unproven. Prior to the second voting question addressing coverage the committee discussed potential criteria for coverage. A majority of the committee voted to not cover bronchial thermoplasty for asthma.

Limitations

NA

Action

The committee checked for availability of a Medicare national coverage decision (NCD). There is no NCD for bronchial thermoplasty for asthma.

The committee discussed clinical guidelines identified for bronchial thermoplasty for asthma from the following organizations:

British Thoracic Society, (2011)

European Respiratory Society, (2014)

American Thoracic Society, (2015)

Global Initiative for Asthma, (2015)

National Institute for Health and Care Excellence, (2012)

The chair noted consistency with some guidelines as long term safety and efficacy have not been established.

The committee chair directed HTA staff to prepare a findings and decision document on bronchial thermoplasty for asthma reflective of the majority vote for public comment followed byfinal approval at the next public meeting.

Health Technology Clinical Committee Authority:

Washington State's legislature believes it is important to use a science-based, clinician-centered approach for difficult and important health care benefit decisions. Pursuant to chapter 70.14 RCW, the legislature has directed the Washington State Health Care Authority (HCA), through its Health Technology Assessment (HTA) program, to engage in an evaluation process that gathers and assesses the quality of the latest medical evidence using a scientific research company and that takes public input at all stages.

Pursuant to RCW 70.14.110 a Health Technology Clinical Committee (HTCC) composed of eleven independent health care professionals reviews all the information and renders a decision at an open public meeting. The Washington State HTCC determines how selected health technologies are covered by several state agencies (RCW 70.14.080-140). These technologies may include medical or surgical devices and procedures, medical equipment, and diagnostic tests. HTCC bases its decisions on evidence of the technology's safety, efficacy, and cost effectiveness. Participating state agencies are required to comply with the decisions of the HTCC. HTCC decisions may be re-reviewed at the determination of the HCA Administrator.