JPPT

Continuing Education

Asthma Review for Pharmacists Providing Asthma Education

Stacie J. Lampkin, PharmD,[1] Cheryl A. Maslouski, PharmD,[2] William A. Maish, PharmD,[3] and Barnabas M. John, PharmD[4]

[1]D'Youville College School of Pharmacy, Buffalo, New York; [2]Nationwide Children's Hospital, Columbus, Ohio; [3]Department of Pharmacy, Arnold Palmer Medical Center, University of Florida College of Pharmacy, Orlando, Florida; [4]Clinical and Administrative Sciences, University of Oklahoma, College of Pharmacy Tulsa, Oklahoma and the University of Oklahoma School of Community Medicine, Tulsa, Oklahoma

Asthma is the most common pediatric illness affecting more than 6 million children in the United States. Children with asthma have more frequent office visits and hospitalizations compared with adults. Despite advances in therapies, asthma still has a significant effect on the health care system. Regardless of the setting, pharmacists are uniquely equipped with an intimate knowledge of medications. With this knowledge, they can provide education to patients at various points throughout the health care system, from hospitalization to office visits to point of pick up at the pharmacy. The goal of this article is to equip the pharmacist with the necessary knowledge to provide education to these patients in a variety of practice settings, including community pharmacies, ambulatory care settings, and during transitions in care.

INDEX TERMS: asthma, guidelines, medications, pediatric, treatment

J Pediatr Pharmacol Ther 2016;21(5):444–471

INTRODUCTION

Asthma is a dynamic, chronic disorder of the lungs involving airway obstruction, caused by inflammation and hyperresponsiveness. The interactions of these features lead to the classic recurrent and reversible symptoms of wheezing, shortness of breath, cough, and tightness in the chest. There are varying degrees of asthma severity, and every patient's condition will fluctuate during his or her lifetime.[1]

Despite more than 20 years of advancement in diagnosis and management, asthma continues to impose social and financial burdens in the United States. Asthma is the most common pediatric chronic disease and affects more than 6 million children in the United States.[1] According to 2012 National Health Interview Survey (NHIS) data, the prevalence of asthma is higher in children (9.3%) than it is in adults (8%), with children 0 to 4 years old having the highest prevalence of acute asthma exacerbations (60.8%), followed by patients 5 to 14 years old (56.3%). Although the rate of asthma exacerbations reported in children is 55.2%, it should be noted that variations by age have been reported.[2,3] In 2010, children had more emergency department (ED) visits, hospitalizations, and urgent care (UC) visits for asthma than did adults.[4] Fortunately, pediatric asthma deaths are rare, but the probability increases as a person with asthma grows older.[4]

When compared with adults who had asthma, children had more routine office visits for asthma care and were more likely to receive education on asthma self-management. Aspects of self-management taught to children included how to recognize signs and symptoms of asthma, manage an exacerbation, and use an inhaler. In addition, children also received an asthma action plan (AAP). Providing appropriate medications and self-management education to patients at a young age, and as frequently as possible in all health care settings, promotes good asthma care and decreases the possibility of death.[4] Repeated education on a consistent basis, such as when a patient goes to the pharmacy every month to refill daily controller therapies, reduces the use of emergent health care services and hospitalizations, improves quality of life and perceived asthma control, and decreases health

Table 1. Learning Objectives for the Educational Session

Upon completion of this program, the practitioner will be able to
1. Identify asthma severity, control, and step therapy using the current 2007 NHLBI guideline tables.
2. Describe how commonly used asthma medications affect asthma pathophysiology.
3. Explain to a patient and caregiver the proper use of the following medication classes in asthma care: quick relievers, ICSs, oral steroids, LABAs, and LTRAs.
4. Explain to a patient and caregiver at least 3 side effects or concerns with common medications used in asthma care.
5. Teach a patient and caregiver to properly use and clean an MDI, VHC or spacer, and nebulizer according to manufacturer specifications.
6. Create an AAP, according to 2007 NHLBI guidelines, which includes appropriate controller(s), rescue medication, symptoms, and patient-specific triggers.

AAP, asthma action plan; ICS, inhaled corticosteroid; LABA, long-acting β-agonist; LTRA, leukotriene receptor antagonist; MDI, metered dose inhaler; NHLBI, National Heart, Lung, and Blood Institute; VHC, valved holding chamber

care spending on asthma.[1] To provide adequate education, pharmacists need an understanding of the 1) Basic pathophysiology of asthma; 2) Asthma severity, level of control, and choice of therapy; 3) Difference among commonly used asthma medications; 4) Appropriate asthma-device technique; and 5) AAPs. Achievement of the objectives associated with this article (Table 1) will enhance skills and knowledge of pharmacists providing asthma education by providing information and clinical pearls around these key elements of learning.

PATHOPHYSIOLOGY

Although no single cause has been identified as leading to a diagnosis of asthma, several factors in combination have been suggested.[5] Currently, it is believed that both genetics and a variety of environmental factors contribute to the development of asthma. Manifestations of asthma can be triggered by numerous factors, including cigarette smoke, dust mites, cockroach allergens, and mold.[5] Bronchoconstriction and inflammation, key targets for pharmacotherapy, are the primary mechanisms that lead to symptoms of cough, wheezing, dyspnea, and chest tightness.[5,6] During an acute exacerbation of asthma, narrowing of the airways and contraction of the smooth muscles occur, which can cause significant morbidity and mortality.[1] Factors that have been related to increased risk of mortality include severe airflow obstruction, 2 or more visits to the ED, and several psychosocial factors.[1] Several inflammatory mediators, including eosinophils, neutrophils, mast cells, and lymphocytes, are involved in the process. In addition, in the lungs and airways, cells release leukotrienes (LTs), a chemoreactant and target for medication therapy in asthma.[7]

SEVERITY, CONTROL, AND CHOICE OF THERAPY

Assessing asthma severity or control is crucial to determine appropriate therapy. *Severity* is assessed when a patient has not been on a controller therapy and can be classified as intermittent, mild persistent, moderate persistent, and severe persistent asthma. *Control* is assessed when a patient has been on controller therapy for at least 4 to 6 weeks and is classified as well controlled, not well controlled, and very poorly controlled asthma.[1]

Severity and Control

Asthma severity is classified by assessing impairment and risk. Impairment is assessed through patient history questions and pulmonary function tests (PFTs). Several tools are validated and available to assist in obtaining this information, including the Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), and the Asthma Therapy Assessment Questionnaire (ATAQ).[1] Additionally, a verbal asthma history should be completed and should be compared with the questionnaire used by asking questions to determine how asthma affected the patient during the past month. Questions should relate to asthma history and to the components of severity or control found on Table 2.

The answers to the above questions are based on evidence and are quantifiable, in contrast to qualitative answers that may be provided (e.g.

Table 2. Potential Questions to Be Asked for an Asthma History

1. In the last month, how many days have you had symptoms while awake?
2. In the last month, how many nights during the week do you wake up because of asthma symptoms?
3. In the last month, how many days have you used a rescue medication, and how many times a day is it used?
4. In the last month, have you had asthma symptoms during exercise or physical activity, and how much (none, minor, some, or extremely) did this limit your activity?

"It is not that bad," "It is nothing like it used to be," or "It's nothing like his brother").[1] Qualitative answers can be misleading and difficult to interpret. Furthermore, if PFTs are available, they may be incorporated into the asthma-impairment assessment, but these are typically unreliable and difficult to obtain in patients younger than 5 years. Next, *future risk* is assessed by determining the number of oral steroid courses in the previous year and considering the severity of, and interval since, the last exacerbation. Assessing risk is more challenging and the effect of severity of, and interval since the last exacerbation, on risk may vary by provider. Regardless, asthma severity or control is ultimately determined by the highest-rated component from both the impairment and risk components.[1]

Assessing asthma control is a similar process to the initial severity determination and is used to assess control for those who are currently and regularly taking controller medications. The assessment questions are the same, but the ratings are different.

Based on the information obtained from a detailed history, the asthma guidelines (Figures 1-6) are used to determine a patient's severity or level of asthma control. The guideline are stratified by patients 5 to 11-years-old (Figures 1 and 2), 0 to 4-years-old (Figures 3 and 4), and those older than 12 years of age (Figures 5 and 6). Use of the appropriate table for patient age is essential as use of the wrong table may result in an inaccurate assessment and ultimately inappropriate treatment.

Case: Part 1

Chief Complaint (CC): Physical, establish care

History of Present Illness (HPI): 5-year-old (28 kg) female moved with family to midwestern part of the United States.

When the asthma flares, the asthma symptoms may become as severe as heavy breathing, coughing, wheezing, and sometimes posttussive emesis. Daytime symptoms occur 3 times/wk. Nighttime symptoms occur 2 times/wk. Symptoms also occur sometimes with physical activity; mother reports it leads to some impairment.

Albuterol is used 1 time/day about 3 to 4 days/wk. It helps her symptoms, but it may take a while to take effect. She has had "many" visits to an ED in the past year requiring bursts of oral steroids (this is the third); the other 2 bursts were 10 and 12 months ago.

She has not been admitted to the hospital for her asthma. Eczema has been quiescent.

Past Medical History (PMH): Food allergies (soy, peanuts, milk, fish, wheat, egg), allergic to dust, severe eczema, and asthma.

Family History (FHx): Siblings with allergies, mother with asthma as a child, but she's outgrown it.

Allergies: As above, environmental

Medications:

- Albuterol hydrofluoroalkane (HFA) metered-dose inhaler (MDI), 2 puffs every (q) 4 hr as needed (prn) for wheezing, short of breath, cough
- Albuterol 2.5 mg/3 mL aerosol, 2.5 mg q 4 hr prn for wheezing, short of breath, cough
- Hydrocortisone 1% cream, applied to affected area (AAA) 2 times/day
- Emollient to AAA 2–3 times/day
- Cetirizine 5 mg/5 mL, 5 mg by mouth (po) q day

Questions (see page 467 for answers)**:**

1. Should the asthma severity or control table be used to assess this patient's case?
2. Based on the appropriate table, how would you classify this patient's asthma?

Choice of Therapy

Once an assessment of severity or control is completed, the *step* of therapy is determined by the lower row in Figures 1-6. Figure 7 is then used to determine which class of medications should be initiated. Unless a contraindication exists, all patient regimens, regardless of step, should include an inhaled β-agonist rescue medication. Once a patient is on a controller medication, and control is achieved, the practitioner must correct-

Components of Severity		Classification of Asthma Severity (5–11 years of age)			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3–4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC >85%	• FEV_1 = >80% predicted • FEV_1/FVC >80%	• FEV_1 = 60–80% predicted • FEV_1/FVC = 75–80%	• FEV_1 <60% predicted • FEV_1/FVC <75%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note) →		
		← Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. →			
		Relative annual risk of exacerbations may be related to FEV_1.			
Recommended Step for Initiating Therapy (See figure 4–1b for treatment steps.)		Step 1	Step 2	Step 3, medium-dose ICS option	Step 3, medium-dose ICS option, or step 4
				and consider short course of oral systemic corticosteroids	
		In 2–6 weeks, evaluate level of asthma control that is achieved, and adjust therapy accordingly.			

EIB, exercise-induced bronchospasm; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; ICS, inhaled corticosteroids

Notes

- The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.
- Level of severity is determined by both impairment and risk. Assess impairment domain by patient's/caregiver's recall of the previous 2–4 weeks and spirometry. Assign severity to the most severe category in which any feature occurs.
- At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma severity. In general, more frequent and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate greater underlying disease severity. For treatment purposes, patients who had ≥2 exacerbations requiring oral systemic corticosteroids in the past year may be considered the same as patients who have persistent asthma, even in the absence of impairment levels consistent with persistent asthma.

Figure 1. Classifying asthma severity and initiating treatment in children 5-11 years of age who are not currently taking long-term control medication[1]

ly determine which step the patient is currently on and then step therapy up or down. Stepping down should be considered when a patient's asthma has been well controlled for at least 3 months. Regardless of control, some patients may always require a controller medication; hence, the decision to step down is patient specific. At each opportunity, health care providers must reassess adherence to therapy, inhaler technique, environmental control, and comorbid conditions. If these factors are not adequately addressed, a patient may continue to be poorly controlled even with therapy being stepping up.[1] The choice of controller brand is often dictated by the agent(s) covered by insurance and the choice of controller type (metered dose inhaler versus dry powder inhaler versus nebulizer) is dependent on the patient's ability to use proper technique.

Components of Control		Classification of Asthma Control (5–11 years of age)		
		Well Controlled	Not Well Controlled	Very Poorly Controlled
Impairment	Symptoms	≤2 days/week but not more than once on each day	>2 days/week or multiple times on ≤2 days/week	Throughout the day
	Nighttime awakenings	≤1x/month	≥2x/month	≥2x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week	Several times per day
	Lung function • FEV_1 or peak flow • FEV_1/FVC	 >80% predicted/ personal best >80%	 60–80% predicted/ personal best 75–80%	 <60% predicted/ personal best <75%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year	≥2/year (see note)	
		Consider severity and interval since last exacerbation		
	Reduction in lung growth	Evaluation requires long-term followup.		
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.		
Recommended Action for Treatment **(See figure 4–1b for treatment steps.)**		• Maintain current step. • Regular followup every 1–6 months. • Consider step down if well controlled for at least 3 months.	• Step up at least 1 step and • Reevaluate in 2–6 weeks. • For side effects: consider alternative treatment options.	• Consider short course of oral systemic corticosteroids, • Step up 1–2 steps, and • Reevaluate in 2 weeks. • For side effects, consider alternative treatment options.

EIB, exercise-induced bronchospasm; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity

Notes:

- The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.
- The level of control is based on the most severe impairment or risk category. Assess impairment domain by patient's/caregiver's recall of previous 2–4 weeks and by spirometry/or peak flow measures. Symptom assessment for longer periods should reflect a global assessment such as inquiring whether the patient's asthma is better or worse since the last visit.
- At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma control. In general, more frequent and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate poorer disease control. For treatment purposes, patients who had ≥2 exacerbations requiring oral systemic corticosteroids in the past year may be considered the same as patients who have persistent asthma, even in the absence of impairment levels consistent with persistent asthma.
- Before step up in therapy:
  - Review adherence to medications, inhaler technique, environmental control, and comorbid conditions.
  - If alternative treatment option was used in a step, discontinue it and use preferred treatment for that step.

Figure 2. Assessing asthma control and adjusting therapy in children 5-11 years of age[1]

Case: Part 2

Question 3 (see page 467 for answer)**:**

For the same 5-year-old patient and her severity level of moderate, persistent asthma, what therapy should be initiated?

PHARMACOTHERAPY

There are 2 broad classifications of inhaled medications: quick-relief medications and controller medications. There are also 2 common oral

Components of Severity		Classification of Asthma Severity (0–4 years of age)			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	0	1–2x/month	3–4x/month	>1x/week
	Short-acting beta$_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year	≥2 exacerbations in 6 months requiring oral systemic corticosteroids, or ≥4 wheezing episodes/1 year lasting >1 day AND risk factors for persistent asthma		
		← Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time. → Exacerbations of any severity may occur in patients in any severity category.			
Recommended Step for Initiating Therapy (See figure 4–1a for treatment steps.)		Step 1	Step 2	Step 3 and consider short course of oral systemic corticosteroids	
		In 2–6 weeks, depending on severity, evaluate level of asthma control that is achieved. If no clear benefit is observed in 4–6 weeks, consider adjusting therapy or alternative diagnoses.			

EIB, exercise-induced bronchospasm

Notes

- The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.
- Level of severity is determined by both impairment and risk. Assess impairment domain by patient's/caregiver's recall of previous 2–4 weeks. Symptom assessment for longer periods should reflect a global assessment such as inquiring whether the patient's asthma is better or worse since the last visit. Assign severity to the most severe category in which any feature occurs.
- At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma severity. For treatment purposes, patients who had ≥2 exacerbations requiring oral systemic corticosteroids in the past 6 months, or ≥4 wheezing episodes in the past year, and who have risk factors for persistent asthma may be considered the same as patients who have persistent asthma, even in the absence of impairment levels consistent with persistent asthma.

Figure 3. Classifying asthma severity and initiating treatment in children 0-4 years of age who are not currently taking long-term control medication[1]

medications used for the treatment and control of asthma: oral steroids and LT modifiers.

Quick-Relief Medications

Short-acting β-agonists (SABAs) and anticholinergics are 2 classes of medications that can be considered quick-relief medications or rescue medications. These are used to treat asthma exacerbations and acute symptoms caused by bronchoconstriction.[1]

The SABAs, such as albuterol and levalbuterol, are the quick-relief medications of choice over anticholinergics.[1] These bronchodilators provide relief of symptoms by relaxing bronchial

Components of Control		Classification of Asthma Control (0–4 years of age)		
		Well Controlled	**Not Well Controlled**	**Very Poorly Controlled**
Impairment	Symptoms	≤2 days/week	>2 days/week	Throughout the day
	Nighttime awakenings	≤1x/month	>1x/month	>1x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week	Several times per day
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year	2–3/year	>3/year
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.		
Recommended Action for Treatment (See figure 4–1a for treatment steps.)		• Maintain current treatment. • Regular followup every 1–6 months. • Consider step down if well controlled for at least 3 months.	• Step up (1 step) and • Reevaluate in 2–6 weeks. • If no clear benefit in 4–6 weeks, consider alternative diagnoses or adjusting therapy. • For side effects, consider alternative treatment options.	• Consider short course of oral systemic corticosteroids, • Step up (1–2 steps), and • Reevaluate in 2 weeks. • If no clear benefit in 4–6 weeks, consider alternative diagnoses or adjusting therapy. • For side effects, consider alternative treatment options.

EIB, exercise-induced bronchospasm

Notes:

- The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.
- The level of control is based on the most severe impairment or risk category. Assess impairment domain by caregiver's recall of previous 2–4 weeks. Symptom assessment for longer periods should reflect a global assessment such as inquiring whether the patient's asthma is better or worse since the last visit.
- At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma control. In general, more frequent and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate poorer disease control. For treatment purposes, patients who had ≥2 exacerbations requiring oral systemic corticosteroids in the past year may be considered the same as patients who have not-well-controlled asthma, even in the absence of impairment levels consistent with not-well-controlled asthma.
- Before step up in therapy:
  - Review adherence to medications, inhaler technique, and environmental control.
  - If alternative treatment option was used in a step, discontinue it and use preferred treatment for that step.

Figure 4. Assessing asthma control and adjusting therapy in children 0-4 years of age[1]

smooth muscle through action on β2-receptors.[8] Patients may perceive that daily SABA use is more effective than daily controller medications because SABAs provide immediate relief of symptoms. However, SABAs do not affect the underlying mechanism of asthma control and use more than twice per week indicates an uncontrolled disease.[1,9] Frequent SABA use is also associated with a small degree of tachyphylaxis (potentially through down-regulation of receptors) to the bronchodilator response.[9] Inhaled SABAs cause few side effects, but tachycardia

Components of Severity		Classification of Asthma Severity ≥12 years of age			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment Normal FEV_1/FVC: 8–19 yr 85% 20 –39 yr 80% 40 –59 yr 75% 60 –80 yr 70%	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3–4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily, and not more than 1x on any day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 >60% but <80% predicted • FEV_1/FVC reduced 5%	• FEV_1 <60% predicted • FEV_1/FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note)		
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category.			
		Relative annual risk of exacerbations may be related to FEV_1.			
Recommended Step for Initiating Treatment (See figure 4–5 for treatment steps.)		Step 1	Step 2	Step 3 and consider short course of oral systemic corticosteroids	Step 4 or 5
		In 2–6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.			

FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; ICU, intensive care unit

Notes:

- The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.
- Level of severity is determined by assessment of both impairment and risk. Assess impairment domain by patient's/caregiver's recall of previous 2–4 weeks and spirometry. Assign severity to the most severe category in which any feature occurs.
- At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma severity. In general, more frequent and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate greater underlying disease severity. For treatment purposes, patients who had ≥2 exacerbations requiring oral systemic corticosteroids in the past year may be considered the same as patients who have persistent asthma, even in the absence of impairment levels consistent with persistent asthma.

Figure 5. Classifying asthma severity and initiating treatment in youths ≥ 12 years of age and adults who are not currently taking long-term control medications[1]

may occur. Levalbuterol, the (*R*)-enantiomer of racemic albuterol, mechanistically may provide greater bronchodilation and less tachycardia than racemic albuterol.[10,11] A meta-analysis comparing levalbuterol to albuterol found no statistically significant difference for respiratory rate, oxygen saturations, and duration of ED care.[12] There was a significantly lower hospital admission rate in the levalbuterol group with an odds ratio of 0.76. There was no difference in occurrence of nausea, vomiting, tremors, jitteriness, headache, and nervousness. Currently, there is mixed evidence demonstrating clinical superiority of levalbuterol over albuterol in efficacy, safety, and cost; therefore, albuterol remains the mainstay SABA.[11–14]

Inhaled anticholinergics cause bronchodilation by blocking the action of acetylcholine at parasympathetic sites in bronchial smooth muscle.[8] Although ipratropium is the only available short-acting anticholinergic, it has a limited role as a quick-relief medication in asthma and should be reserved as an alternative for patients

Components of Control		Classification of Asthma Control (≥12 years of age)		
		Well Controlled	Not Well Controlled	Very Poorly Controlled
Impairment	Symptoms	≤2 days/week	>2 days/week	Throughout the day
	Nighttime awakenings	≤2x/month	1–3x/week	≥4x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week	Several times per day
	FEV_1 or peak flow	>80% predicted/ personal best	60–80% predicted/ personal best	<60% predicted/ personal best
	Validated questionnaires ATAQ ACQ ACT	 0 ≤0.75* ≥20	 1–2 ≥1.5 16–19	 3–4 N/A ≤15
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year	≥2/year (see note)	
		Consider severity and interval since last exacerbation		
	Progressive loss of lung function	Evaluation requires long-term followup care		
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.		
Recommended Action for Treatment (see figure 4–5 for treatment steps)		• Maintain current step. • Regular followups every 1–6 months to maintain control. • Consider step down if well controlled for at least 3 months.	• Step up 1 step and • Reevaluate in 2–6 weeks. • For side effects, consider alternative treatment options.	• Consider short course of oral systemic corticosteroids, • Step up 1–2 steps, and • Reevaluate in 2 weeks. • For side effects, consider alternative treatment options.

*ACQ values of 0.76–1.4 are indeterminate regarding well-controlled asthma.

EIB, exercise-induced bronchospasm; ICU, intensive care unit

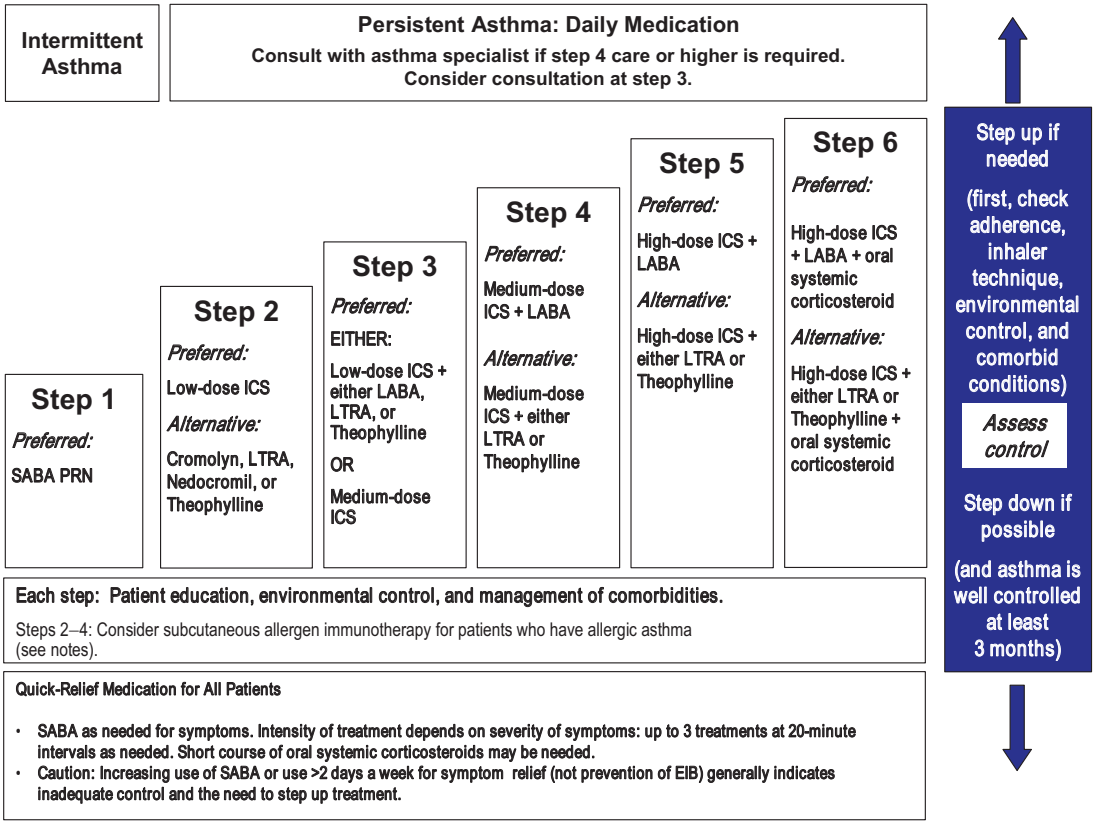
Notes:

- The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.
- The level of control is based on the most severe impairment or risk category. Assess impairment domain by patient's recall of previous 2–4 weeks and by spirometry/or peak flow measures. Symptom assessment for longer periods should reflect a global assessment, such as inquiring whether the patient's asthma is better or worse since the last visit.
- At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma control. In general, more frequent and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate poorer disease control. For treatment purposes, patients who had ≥2 exacerbations requiring oral systemic corticosteroids in the past year may be considered the same as patients who have not-well-controlled asthma, even in the absence of impairment levels consistent with not-well-controlled asthma.
- Validated Questionnaires for the impairment domain (the questionnaires do not assess lung function or the risk domain)
  - ATAQ = Asthma Therapy Assessment Questionnaire© (See sample in "Component 1: Measures of Asthma Assessment and Monitoring.")
  - ACQ = Asthma Control Questionnaire© (user package may be obtained at www.qoltech.co.uk or juniper@qoltech.co.uk)
  - ACT = Asthma Control Test™ (See sample in "Component 1: Measures of Asthma Assessment and Monitoring.")
  - Minimal Important Difference: 1.0 for the ATAQ; 0.5 for the ACQ; not determined for the ACT.
- Before step up in therapy:
  - Review adherence to medication, inhaler technique, environmental control, and comorbid conditions.
  - If an alternative treatment option was used in a step, discontinue and use the preferred treatment for that step.

Figure 6. Assessing asthma control and adjusting therapy in youths ≥ 12 years of age or adults[1]

who cannot tolerate SABAs.[1] Ipratropium may also provide an additive benefit to SABAs in moderate to severe asthma exacerbations in the ED setting.[1]

Regardless of which quick-relief medication a patient has been prescribed, it is important to educate all patients about the role of their rescue medication. This includes the difference between quick-relief and controller medications and the need to see their health care provider if they are using their rescue medication more than twice per week to treat asthma symptoms.



Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy. ICS, inhaled corticosteroid; LABA, inhaled long-acting beta$_2$-agonist, LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta$_2$-agonist

Notes:

- The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.
- If alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.
- Theophylline is a less desirable alternative due to the need to monitor serum concentration levels.
- Step 1 and step 2 medications are based on Evidence A. Step 3 ICS + adjunctive therapy and ICS are based on Evidence B for efficacy of each treatment and extrapolation from comparator trials in older children and adults—comparator trials are not available for this age group; steps 4–6 are based on expert opinion and extrapolation from studies in older children and adults.
- Immunotherapy for steps 2–4 is based on Evidence B for house-dust mites, animal danders, and pollens; evidence is weak or lacking for molds and cockroaches. Evidence is strongest for immunotherapy with single allergens. The role of allergy in asthma is greater in children than in adults. Clinicians who administer immunotherapy should be prepared and equipped to identify and treat anaphylaxis that may occur.

Figure 7. Stepwise approach for managing asthma in children 5-11 years of age[1]

Steroids in Asthma

Steroids are considered the most potent and effective available anti-inflammatory medications. They block late-phase reaction to allergens, reduce hyperresponsiveness, and inhibit inflammatory cell migration and inflammation. Steroids have not been proven to change the underlying pathophysiology of the lungs nor progression of the disease. However, they can improve quality of life by controlling current symptoms and preventing exacerbations or decreasing the intensity of exacerbations. Oral steroids and inhaled steroids are both used in asthma treatment regimens, but they have different roles in therapy.[1]

Table 3. Inhaled Corticosteroids for Use in Children—US Food and Drug Administration Versus National Asthma Education and Prevention Program

Active Ingredient	FDA-Approved Age Indication,[37] yr	Dosing Allowed for Younger Ages[1]
Beclomethasone	5 or older	No
Budesonide inhalation suspension	1-8	Yes (0-4 yr)
Budesonide dry powder	6 or older	Yes (5 yr)
Ciclesonide	12 or older	No
Fluticasone (MDI only)	4 or older	Yes (0-4 yr)
Mometasone	4 or older	No

MDI, metered dose inhaler

Inhaled Steroids

Inhaled corticosteroids (ICSs) are the backbone of daily preventative care and are used on a daily basis. The ICSs have the advantage of being deposited in the lungs and working at the site of airway swelling and inflammation. Regular use of ICS is associated with improved ciliary beat, improved epithelium, and less inflammatory mediators in the basement membranes.[15] They have minimal bioavailability, so very little is absorbed from the lungs into the systemic circulation. For these reasons, ICS are safe and effective for long-term use to control asthma symptoms and prevent exacerbations. The use of doubling ICS doses to manage flares at home is not recommended based on limited data showing benefit.[1,16] Using larger doses of ICS for management of asthma flares has been studied and recommendations published by a workgroup of asthma and allergy experts. The practice of quadrupling the total daily dose of ICS in children may prevent asthma exacerbations and severity of symptoms of exacerbations. This type of management, however, did not show a difference in the rate of use of systemic steroids to treat exacerbations in patients treated with large versus small doses of ICS. The expert group also addresses the use of ICS combined with long-acting β-agonists (LABA) as maintenance therapy and additional as-needed doses of the same combination for asthma flares. The use of this step-up dosing in children has not been well studied. Furthermore, the studies looking at this type of management noticed the higher doses of ICS caused decreased growth in children. Therefore, the use of ICS plus LABA as maintenance and as-needed doses to treat exacerbations is not recommended.[17]

There are several ICS dosage forms available. Although many are not approved by the US Food and Drug Administration (FDA) for pediatric use, certain ones are recommended in the guidelines to be used in children (Table 3).[1] These ICSs and their specific doses can be found in Figure 8.[1] Delivery systems for the various products are discussed later.

The side effects of ICS are local, when properly used with a valved holding chamber (VHC) or with proper inhaler technique. Sore throat, hoarseness in the voice, dry mouth, and thrush are most commonly reported. Thrush is due to deposition of the medication in the oropharynx; the proper use of a VHC with mask or mouthpiece and rinsing the mouth after use minimizes the oral side effects associated with ICS. Reductions in growth velocity have also been reported, but this does not include a significant decrease in overall stature.[1] Studies have shown that final height in patients who use ICS is still within millimeters of expected height.[18] More systemic side effects are rare and are usually associated with chronic higher doses. These include adrenal suppression, osteoporosis, easy bruising, and thinning of the skin.[1] For these reasons, long-term treatment should consist of the lowest possible dose, weighing the benefits of asthma control with ICS adverse events.

Oral Steroids

Oral steroids are given as a short burst to quickly decrease pulmonary swelling and inflammation that cause asthma exacerbations and to prevent progression of acute disease. They have been shown to reduce hospitalization and relapse due to acute exacerbations and to improve pulmonary function.[19] As discovered in practice, some patients and parents report they like the quick resolution of symptoms with oral steroids

Drug	Low Daily Dose		Medium Daily Dose		High Daily Dose	
	Child 0–4	Child 5–11	Child 0–4	Child 5–11	Child 0–4	Child 5–11
Beclomethasone HFA						
40 or 80 mcg/puff	NA	80–160 mcg	NA	>160–320 mcg	NA	>320 mcg
Budesonide DPI						
90, 180, or 200 mcg/inhalation	NA	180–400 mcg	NA	>400–800 mcg	NA	>800 mcg
Budesonide inhaled						
Inhalation suspension for nebulization (child dose)	0.25–0.5 mg	0.5 mg	>0.5–1.0 mg	1.0 mg	>1.0 mg	2.0 mg
Flunisolide						
250 mcg/puff	NA	500–750 mcg	NA	1,000–1,250 mcg	NA	>1,250 mcg
Flunisolide HFA						
80 mcg/puff	NA	160 mcg	NA	320 mcg	NA	≥640 mcg
Fluticasone						
HFA/MDI: 44, 110, or 220 mcg/puff	176 mcg	88–176 mcg	>176–352 mcg	>176–352 mcg	>352 mcg	>352 mcg
DPI: 50, 100, or 250 mcg/inhalation	NA	100–200 mcg	NA	>200–400 mcg	NA	>400 mcg
Mometasone DPI						
200 mcg/inhalation	NA	NA	NA	NA	NA	NA
Triamcinolone acetonide						
75 mcg/puff	NA	300–600 mcg	NA	>600–900 mcg	NA	>900 mcg

HFA, hydrofluoroalkane; NA, not approved and no data available for this age group

Notes:

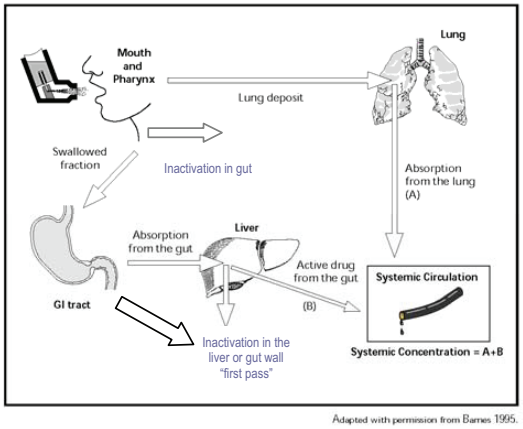
- **The most important determinant of appropriate dosing is the clinician's judgment of the patient's response to therapy.** The clinician must monitor the patient's response on several clinical parameters and adjust the dose accordingly. The stepwise approach to therapy emphasizes that once control of asthma is achieved, the dose of medication should be carefully titrated to the minimum dose required to maintain control, thus reducing the potential for adverse effect.
- Some doses may be outside package labeling, especially in the high-dose range. Budesonide nebulizer suspension is the only ICS with FDA approved labeling for children <4 years of age.
- Metered-dose inhaler (MDI) dosages are expressed as the actuator dose (the amount of the drug leaving the actuator and delivered to the patient), which is the labeling required in the United States. This is different from the dosage expressed as the valve dose (the amount of drug leaving the valve, not all of which is available to the patient), which is used in many European countries and in some scientific literature. Dry powder inhaler (DPI) doses are expressed as the amount of drug in the inhaler following activation.
- For children <4 years of age: The safety and efficacy of ICSs in children <1 year has not been established. Children <4 years of age generally require delivery of ICS (budesonide and fluticasone HFA) through a face mask that should fit snugly over nose and mouth and avoid nebulizing in the eyes. Wash face after each treatment to prevent local corticosteroid side effects. For budesonide, the dose may be administered 1–3 times daily. Budesonide suspension is compatible with albuterol, ipratropium, and levalbuterol nebulizer solutions in the same nebulizer. Use only jet nebulizers, as ultrasonic nebulizers are ineffective for suspensions.
- For fluticasone HFA, the dose should be divided 2 times daily; the low dose for children <4 years is higher than for children 5–11 years of age due to lower dosedelivered with face mask and data on efficacy in young children.

Figure 8. Estimated comparative daily dosage of inhaled corticosteroids in children[1]

and may erroneously refer to them as "cough medicines."

The oral steroids of choice are prednisone or prednisolone.[8] Oral liquid steroids are difficult to administer to children because of the strong bitter taste and burning after-taste. Therefore, prednisone tablets are preferred for older children able to swallow solid dosage forms. The introduction of prednisolone sodium phosphate liquid (Orapred [Concordia Pharmaceuticals, Oakville, ON, Canada] brand grape flavor and other fairly palatable generics) offers better-received forms of

- Comparative dosages are based on published comparative clinical trials (Adams et al. 2005; Barnes et al. 1998; Kelly 1998; Lasserson et al. 2005; Pedersen and O'Byrne 1997). The rationale for some key comparisons is summarized as follows:
  - The high dose is the dose that appears likely to be the threshold beyond which significant hypothalamic-pituitary-adrenal (HPA) axis suppression is produced, and, by extrapolation, the risk is increased for other clinically significant systemic effects if used for prolonged periods of time (Martin et al. 2002; Szefler et al. 2002).
  - The low- to medium-doses reflect findings from dose-ranging studies in which incremental efficacy within the low- to medium dose ranges was established without increased systemic effect as measured by overnight cortisol excretion. The studies demonstrated a relatively flat dose-response curve for efficacy at the medium-dose range; that is, increasing the dose of high-dose range did not significantly increase efficacy but did increase systemic effect (Adams et al. 2001; Martin et al. 2002; Szefler et al. 2002).
  - The doses for budesonide and fluticasone MDI or DPI are based on recently available comparative data. These new data, including meta-analyses, show that fluticasone requires one-half the microgram dose of budesonide DPI to achieve comparable efficacy (Adams et al. 2005; Barnes et al. 1998; Nielsen and Dahl 2000).
  - The dose for beclomethasone in HFA inhaler should be approximately one-half the dose for beclomethasone chlorofluorocarbon (CFC) inhaler for adults and children, based on studies demonstrating that the different pharmaceutical properties of the medications result in enhanced lung delivery for the HFA (a less forceful spray from the HFA propellant and a reengineered nozzle that allows a smaller particle size) and clinical trials demonstrating similar potency to fluticasone at 1:1 dose ratio (Boulet et al. 2004; Busse et al. 1999; Gross et al. 1999; Lasserson et al. 2005; Leach et al. 1998; Pedersen et al. 2002; Szefler et al. 2002; Thompson et al. 1998).
  - The dose for budesonide nebulizer suspension is based on efficacy and safety studies (Baker et al. 1999; Kemp et al. 1999; Shapiro et al. 1998). It is noted that the efficacy studies did not demonstrate a clear or consistent dose-response, although the high dose of 2.0 mg was effective in a placebo-controlled study in 40 infants who had severe asthma (de Blic et al. 1996). In a small, open-label, long-term safety study, the ACTH-stimulated cortisols appeared lower in the 13 infants receiving a high dose of 2.0 mg budesonide compared to infants receiving lower doses, but this result was not statistically significant, perhaps due to the small study size (Scott and Skoner 1999).
  - The dose for flunisolide HFA is based on product information and current literature (Corren et al. 2001; Gillman et al. 2002; Richards et al. 2001).
  - The dose of budesonide/formoterol in children is based on product information and current literature (Pohunek et al. 2006; Tal et al. 2002; Zimmerman et al. 2004).
  - The dose for fluticasone HFA in children <5 years of age is based on clinical studies demonstrating efficacy at this dose of 176 mcg/day (Bisgaard et al. 2004; Guilbert et al. 2006).



Adapted with permission from Barnes 1995.

- **Bioavailability**

  Both the relative potency and the relative bioavailability (systemic availability) determine the potential for systemic activity of an ICS preparation. As illustrated here, the bioavailability of an ICS is dependent on the absorption of the dose delivered to the lungs and the oral bioavailability of the swallowed portion of the dose received.
  - Absorption of the dose delivered to the lungs:
    - Approximately 10–50 percent of the dose from the MDI is delivered to the lungs. This amount varies among preparations and delivery devices.
    - Nearly all of the amount delivered to the lungs is bioavailable.
  - Oral bioavailability of the swallowed portion of the dose received:
    - Approximately 50–80 percent of the dose from the MDI without a spacer or valved holding chamber is swallowed.
    - The oral bioavailability of this amount varies:

      Either a high first-pass metabolism or the use of a spacer/holding chamber with an MDI can decrease oral bioavailability, thus enhancing safety (Lipworth 1995).

      The approximate oral bioavailability of ICS has been reported as: beclomethasone dipropionate, 20 percent; flunisolide, 21 percent; triamcinolone acetonide, 10.6 percent; budesonide, 11 percent; fluticasone propionate, 1 percent; mometasone, <1 percent (Affrime et al. 2000; Chaplin et al. 1980; Check and Kaliner 1990; Clissold and Heel 1984; Davies 1993; Harding 1990; Heald et al. 1995; Martin et al. 1974; Mollmann et al. 1985; Szefler 1991; Wurthwein and Rohdewald 1990).

Potential drug interactions

- A number of the ICSs, including fluticasone, budesonide, and mometasone, are metabolized in the gastrointestinal tract and liver by CYP 3A4 isoenzymes. Potent inhibitors of CYP 3A4, such as ritonavir and ketoconazole, have the potential for increasing systemic concentrations of these ICSs by increasing oral availability and decreasing systemic clearance. Some cases of clinically significant Cushing syndrome and secondary adrenal insufficiency have been reported (Johnson et al. 2006; Samaras et al. 2005).

Figure 8. Estimated comparative daily dosage of inhaled corticosteroids in children[1] (*cont*).

oral steroids in more-concentrated (15 mg/5 mL) solutions compared with the older prednisolone (15 mg/5 mL and 5 mg/5 mL) and prednisone (5 mg/5 mL) solutions. Much of the offending taste was due to the amount of alcohol used in these liquid preparations (5% in prednisolone liquid and 2% in prednisolone sodium phosphate solution).[8] Dexamethasone is another oral steroid used to treat acute asthma exacerbations.[8] Because of its longer half-life, studies have shown that oral dexamethasone, in 1 or 2 doses, works as well as 5 days of prednisolone for mild to moderate exacerbations. Patients on oral dexamethasone have similar rates of unscheduled doctor visits for asthma, hospital admission rates, and vomiting.[20] Children unable to tolerate prednisone or prednisolone may tolerate oral dexamethasone solution, which also tastes poor to most patients, but may be favored for its 1- or 2-dose regimens. However, because of commercial availability and insurance reimbursement, prednisone and prednisolone continue to be the drugs of choice.

Most children may be managed with a 5-day course of oral steroids.[1] A short course, 3 to 10 days, of oral steroid treatment for asthma alleviates the need for a taper. Any patient needing a steroid burst should be seen 1 week later to ensure symptoms have resolved. Initial treatment with oral steroids by ED personnel should be followed with a visit to the patient's primary care provider. Occasionally, a patient may need a standing at-home, short-course regimen of oral steroids. These qualifying patients have severe asthma, may be managed by a pulmonologist or other asthma specialist, or they may live in rural areas and quick emergent care is needed for exacerbations. Oral steroids used in this manner should be included in the patient's asthma action plan. Home use of oral steroids, however, should include a call to the patient's physician.

Compared with ICS, oral steroids are associated with more side effects. During short bursts of therapy, patients may have nausea and vomiting, increased appetite, weight gain, and changes in mood. Long-term use is associated with the previously listed side effects plus adrenal axis suppression, growth suppression, hypertension, diabetes, Cushing syndrome, osteoporosis, muscle weakness, and impaired immune system (an important consideration because children are immunized in early childhood).[1] Additional steroid-counseling points are provided in Table 4.

Long-Acting β-Agonists

Chronic use of LABAs in combination with ICS has demonstrated efficacy in the treatment of asthma in several studies. The LABAs work by selectively binding to β_2 receptors in the lungs, which results in relaxing the smooth muscles in airways for a prolonged period.[8] The onset varies by product. Some studies have reported favorable use of formoterol before exercise to treat exercise-induced bronchospasms (EIBs).[21] Patients should be instructed to use a LABA only as a controller medication and not as a rescue inhaler. Counseling on the correct use of the device and indication is important to avoid confusion. In 2010, in response to an increase in the number of asthma-related deaths, the FDA issued a warning against the use of LABA monotherapy for the treatment of asthma, including in children and adolescents.[22] The use of LABA in combination with inhaled corticosteroids, however, is still recommended and continues to be included in recommendations.[1] Although the use of a LABA as monotherapy is not recommended because of increasing inflammation and down-regulation of β-2 receptors, the use in combination with an ICS is recommended. It is believed that the ICS benefits patients taking a LABA by increasing the number of β_2 receptors and decreasing inflammation.[23] There are no indications for use of LABA monotherapy as a controller in the current guidelines, and alternatives to the addition of LABA are available in all steps. However, when stepping up therapy, the addition of a LABA to ICS has proven to be more effective in many children than the addition of a LT receptor antagonist (LTRA) to ICS or an increase in the ICS dosage.[24] For a list of available LABA products, see Table 5.

LT Modifiers

Medications in the class of LT modifiers include montelukast, zafirlukast, and zileuton. These have many beneficial effects in patients with asthma: improved pulmonary function, increased peak expiratory flow, decreased daytime and nighttime symptoms, reduced need for SABAs, decreased number of asthma flares, and improved quality of life.[7] Montelukast, a LTRA, is the product most frequently used in children with asthma.

The LTRAs are typically used as second- or

Table 4. Patient Counseling Points for Inhaled and Oral Steroids[1,37,38]

Inhaled Steroids	Oral Steroids
• Always use a spacing device for MDIs. • Use every day for best results. • Maximum effect doesn't occur until after 2 wk of daily use. • Do not stop giving the medicine just because your child feels better. • Do not use to treat acute symptoms. • Teach the family proper device technique. • Side effects: thrush, sore throat, hoarse voice, headache. • Rinse mouth after use. • If applicable, follow the dose counter on the inhaler device to determine when to refill and start a new device.	• Give by mouth for the full duration of treatment, even if the child is feeling better. • Call your child's doctor if symptoms get worse or do not improve in 2 days. • Give all doses with food to prevent GI side effects. • May cause moodiness or difficulty sleeping. For once-daily doses, give in the morning. For twice-daily doses, make the last dose no later than the evening meal. • Let your child's doctor know if there is blood in the stool or your child vomits blood. • Talk with your pediatrician about immunizations if your child is on ≥2 mg/kg/day or ≥20 mg/day for >14 days. • Prednisolone sodium phosphate (e.g. Orapred) liquid should be refrigerated. • Dispense liquid formulations with an appropriate measuring device.

GI, gastrointestinal; MDI, metered dose inhaler

third-line therapies or as an add-on to controller therapies that are already in place but not providing the patient an acceptable level of control. This is due to ICS being more effective in the treatment of persistent asthma when compared with LTRAs.[7] However, certain patients have been deemed to respond more favorably to LTRAs than to ICS: those who are younger than 10 years, those with a high level of LTs in the urine (although this is not a laboratory value that is typically used), disease of shorter duration, and cough-variant asthma.[7,25,26] Other instances in which LTRAs may be an alternate first-line choice include patients who cannot or will not use ICS or an inhaler device, those who need additional add-on therapy, those with allergic rhinitis, and those whose symptoms are usually triggered by viral infections.[7] In addition, montelukast has proven to be effective in controlling EIB in patients with only exercise-induced symptoms or those who are not controlled on ICS for their EIB.[24]

The LTRAs are typically well-tolerated, and most side effects are benign. Possible montelukast side effects include headache, ear infection, pharyngitis, abdominal pain, nausea, rash, angioedema, and behavior side effects (insomnia, tremor, depression, anxiety, suicidal ideation).[24] In 2008, the FDA issued a safety alert for the risk of suicide associated with LTRAs.[27] In 2009, manufacturers added this concern to product labeling.[27] One study, conducted by the manufacturer, looked at reports of possible suicidality in randomized, double-blind, placebo-controlled, active-controlled, or open-label clinical trials of montelukast in patients with asthma. There were no suicides completed, and suicidality was rare in montelukast, placebo, and other active-treatment groups.[28] In a similar study looking at behavior-related adverse events in adults and children taking montelukast for asthma, reports of adverse events were infrequent and were similar in montelukast or placebo groups.[29] Schumock et al[27] noted that children or adults with asthma who had attempted suicide while taking a LTRA were at higher risk for doing so if they had a previous attempt, had psychiatric illness or another illness associated with suicide, were taking other medicines that also increased suicide risk, or had more-severe class of asthma. They noted that patients 19 to 24 years old with these risk factors were at a statistically significant

Table 5. Inhaled Products Containing LABAs

Active Ingredient	FDA-Approved Age Indication,[37] yr	Dosing Allowed for Younger Ages[1]
Formoterol DPI aerolizer	5 or older	No
Formoterol/budesonide MDI	12 or older	Yes (0-4 yr)
Formoterol/mometasone MDI	12 or older	Yes (5 yr)
Salmeterol	≥ 12 yrs	No
Salmeterol/fluticasone DPI diskus, MDI	4 or older	Yes (0–4 yr)

DPI, dry-powder inhaler; FDA, Food and Drug Administration; LABA, long-acting β-agonist; MDI, metered-dose inhaler

higher risk for attempting suicide. QuarterWatch (Institute for Safe Medication Practices, Horsham, PA) published a special report[30] on adverse effects of normal medication use in children (age 18 years or younger) for the years 2008 to 2012. Montelukast was ranked second overall, with psychiatric effects occurring more than 25% of the time. Looking at medications that caused only psychiatric side effects, montelukast was first. The organization reported that a surge in reporting in 2008 and a decline by 2012. The authors examined the fewer reports and stated there was still an association between montelukast and psychiatric side effects. The recommendation was to monitor the patient for those effects.[30]

ASTHMA-DEVICE TECHNIQUE

Each of the above products come in varying dosage forms and have their own benefits, care requirements, and delivery techniques.[31,32] Technique for drug delivery should be assessed at each interaction with health care professionals, and teaching should be provided as needed.[1] Inhaled medications can be delivered by several different mechanisms that are used in different ways. Inhalers include pressurized metered dose inhalers (MDIs) that have hydrofluoroalkane (HFA) propellants and dry-powder inhalers (DPIs).[31,32] Most inhalers should be primed before use.[31] Depending on the individual product, inhalers may need to be primed when a new one is obtained from the pharmacy or if the inhaler has not been used for more than 1 to 2 weeks. Refer to individual products' inserts for specific instructions.

Metered-Dose Inhalers

The HFA MDIs should be administered with a VHC and mouthpiece or with a VHC and a mask. Oral MDI technique without a VHC is challenging to master and often results in decreased medication deposition into the lungs.[31,32] Therefore, all patients should be counseled, regardless of age, on the importance of using their MDI with a VHC.

The HFA MDIs with dose counters are especially useful, so it is possible to tell when all the accurate doses have been delivered. When all accurate doses are delivered from devices that have no counters, the device will emit a spray of inactive ingredients but no longer provide full doses. Patients using these products need to keep track of the number of puffs used to determine when there are no longer accurate doses left. Directions for use of MDIs with VHC and mouthpiece or mask can be found in Table 6.

To clean the HFA MDI, the metal canister is removed, the plastic L-shaped boot is washed with water and mild dish detergent, and then the boot is rinsed with a heavy stream of hot water for 30 seconds. The metal tip of the canister should be inspected for residual spray and be wiped clean with a tissue, if necessary.[31] This should be performed weekly when it is being used. The package insert has additional cleaning instructions, and instructions may vary by product.

To clean the VHC with or without mask, it is soaked for at least 15 minutes before the end plastic pieces are washed with water and mild dish detergent, and then the outer pieces are rinsed with water and air dried. The mild dish detergent mixture is placed inside the larger tube and agitated (without rubbing the sides); the inside is not rinsed. The piece is set upright so a thin film of soap dries on the inner sides, which decreases the static electricity that can trap the MDI contents on the wall of the device.[31] The VHCs that have an antistatic coating can be rinsed after cleaning. When dry, the parts are

Table 6. How to Use an MDI with VHC and Mouthpiece or Mask

To Use an MDI With VHC and Mouthpiece
1. Sit or stand up straight.
2. Take off cap, shake inhaler for 10 sec, and place in VHC (if not already in VHC).
3. Exhale completely.
4. Place mouthpiece in mouth.
5. Press down on the inhaler once and inhale slowly for a count of 10. Hold breath 10 sec, wait 1 min, then repeat the entire process, if indicated. Note: 2 puffs at a time into the chamber do not deliver 2 full doses.
6. If the MDI is an ICS, rinse the mouth (with drink, food, or tooth brushing) after use to prevent thrush.
To Use an MDI With VHC and Mask
1. Make sure the mask is appropriate for the patient size. The mask must form a seal and fit over the nose and around the mouth at the same time when placed against the skin (even when patient is smiling).
2. Sit or stand up straight.
3. Take off cap and shake inhaler for 10 seconds and place in VHC (if not already in VHC).
4. Place mask over the nose and mouth.
5. Press down on the inhaler once and breathe in and out 6 times (slowly if possible). Repeat the entire process, if indicated. Note: 2 puffs at a time into the chamber do not deliver 2 full doses.
6. If MDI is an ICS, rinse the mouth (with drink, food, or tooth brushing) after use to prevent thrush.

ICS, inhaled corticosteroids; MDI, metered dose inhaler; VHC, valved holding chamber

reassembled. Many manufacturers recommend weekly cleaning when a VHC is being used.

Dry Powder Inhalers

Different inhalation techniques are used for the various DPI devices. See individual manufacturer information for device-specific details. Some require a rapid and forceful inhalation (e.g., 60 L/min or being inhaled for 1 to 2 seconds). This rate is difficult to produce for most patients younger than 6 years. These devices should not be shaken, and exhaling into the device may displace the powder. Delivery extent may be better than that for MDIs if an excellent technique is used. Only a few grade-school children, however, can master this technique.[33] Most children confuse DPI techniques with the MDI HFA with VHC technique and poorly deliver both medications; for this reason, most patients and parents prefer to keep the technique (e.g., HFA MDI with VHC) the same for rescue and controller medications. A DPI should be kept as dry as possible because moisture may cause clumping of the medications, thus decreasing the respirable fraction.[31]

Aerosol Therapy

Aerosol therapy can often be effectively delivered with a mouthpiece or mask. People often incorrectly use the term *nebulizer* to refer to the combination of the chamber or the cup that holds the medication (the nebulizer) and the electric compressor. The compressor forces air into the nebulizer and causes the medication to form a mist. It may take less time to teach this method, so it is favored by some pediatricians. Some limitations to aerosol therapy are that it is more time consuming to use and clean, the medication is more expensive, and it is inconvenient having to have a power source nearby.[1] Each product's manual should be used for specific instructions before use. However, the general steps for use are listed in Table 7.

The "blow by" technique (i.e., holding the mask or open tube near an infant's nose and mouth to deliver the mist) is incorrect and ineffective. Some studies note a 40% to 85% decrease in deposition with the blow by technique.[34] Crying or fussiness will decrease drug delivery by 75%.[35]

Nebulized albuterol with a compressor has been compared with HFA MDI with a holding chamber in children in many studies with similar results. In one study, children 2 to 9 years old were given an HFA MDI with a low-static holding chamber (Aerochamber with mask [Allergan, Parsippany-Troy Hills, NJ]) and a nebulizer with compressor (Pari LC Star and Pari Proneb TURBO [PARI Respiratory Equipment, Midlothian, VA]).[1,36] There was no difference in the

Table 7. General Steps for Use of Aerosol Therapy

1. Put medication into nebulizer; close nebulizer.
2. Attach mouthpiece or mask to upper end of nebulizer. The mouthpiece is usually used for patients at least 6 yr old.
3. Connect tubing to air outlet on compressor.
4. Sit up straight.
5. Place mouthpiece in mouth or mask on face (covering mouth and nose).
6. Turn on the power for the compressor.
7. Breathe slowly and steadily, occasionally taking deeper breaths with a breath hold, if possible, until most of the medication has been delivered. Depending on the volume being aerosolized, this process takes 10-15 min to deliver a 3-mL treatment.
8. After each treatment, wash all nebulizer and mouth or mask parts (except tubing) in liquid dish soap and water; rinse well with water, then shake off any excess water. Some non-disposable nebulizers can be washed in a dishwasher (see individual manufacturer information). Reattach nebulizer pieces and tubing to the air compressor; turn on compressor to dry nebulizer quickly. Make sure nebulizer is completely dry before storing.
9. Every other treatment day, soak all parts of the nebulizer for 1 hr in a solution of 1 part distilled white vinegar and 3 parts hot water. The solution should be fresh. Remove the parts from the vinegar solution and rinse them in water. Discard the solution. Shake off any excess water. Reattach the nebulizer pieces and tubing to the air compressor and turn on the compressor to dry the nebulizer quickly. Make sure the nebulizer is completely dry before storing.

effectiveness in drug delivery of albuterol (Table 8) between administration methods when correct technique was used. The evidence is so strong from this and other studies that some children's hospitals have stopped using nebulizers with compressors. Many studies indicate that 4 to 8 puffs of albuterol with a VHC produce an equivalent response to 2.5-mg nebulized albuterol.[1,36]

Case: Part 3 (3 Months Later)

For the same 5-yr-old patient:

- Daytime symptoms occur 3 times/wk.
- Nighttime symptoms occur 2 times/wk.
- Symptoms also occur sometimes with physical activity; mother reports these symptoms lead to some impairment.
- Albuterol was used 30 times in the previous month.
- Patient has not needed to return to a physician for asthma.
- Eczema has been quiescent.

Medications:

- Albuterol hydrofluoroalkane (HFA) metered-dose inhaler (MDI), 2 puffs with valved holding chamber (VHC) every (q) 4 hr as needed (prn) for wheezing, shortness of breath, cough
- Albuterol 2.5 mg/3 mL nebulized, 2.5 mg q 4 hr prn wheezing, short of breath, cough
- Fluticasone 44 mcg HFA, 2 puffs with VHC twice a day (BID), every day
- Hydrocortisone 1% cream, applied to affected area (AAA) BID
- Emollient, AAA 2 to 3 times/day
- Cetirizine, 5 mg/5 mL, 5 mg by mouth (po) q day
- No side effects are reported with the medications.

Based on Figure 2, "Assessing Asthma Control and Adjusting Therapy in Children 5–11 Years of Age," the patient appears to have very poorly controlled asthma, despite being started on an inhaled corticosteroid (ICS).

Question 4 (see page 467 for answer).

What additional assessment should be conducted to determine whether this patient is truly poorly controlled?

ASTHMA ACTION PLAN

A written AAP,[1] such as the example in Figure 9, should be provided and reviewed with each patient that is diagnosed with asthma, and every time asthma is addressed at a visit, even if medications are not changed. An AAP is a daily plan used by the patient to monitor daily signs and symptoms of asthma, to assess his or her level of control, and to determine what actions and medications should be taken based on that information. In some instances, AAPs may incorporate a patient's peak flow readings. Peak flow may be used in conjunction with, or

Table 8. Percentage of salbutamol* deposition of in the lungs, comparing administration via nebulizer versus inhaler with spacer[39]

Patient Age, yr	Nebulizer, %	pMDI/VHC, %	p Value
2-4	5.4	5.4	0.96
5-9	11.1	9.6	0.34

pMDI, pressurized metered-dose inhaler; VHC, valved holding chamber
*Salbutamol is the same as albuterol

instead of, symptom assessment in patients with more-severe asthma, poorly controlled asthma, or severe exacerbations. Peak flow monitoring (PFM) is recommended for patients who cannot correctly identify asthma symptoms and prefer objective data to manage their asthma. Keep in mind that PFM is subject to poor information upon which to act because it is dependent upon strong patient effort, proper technique and frequent technique assessment, and professional instruction and demonstrations. Patients who cannot keep the inhalation technique of medications separate from the PFM technique despite education are not typically encouraged to use PFM. The development of an AAP should be the result of a patient-provider partnership and decided upon jointly.

Written AAPs provide an opportunity for clinicians and patients to communicate about asthma so the patient becomes familiar with the disease and what is expected of them. The AAPs empower patients to self-manage their conditions. When part of a well-taught self-management education program, AAPs assist in decreasing ED visits and hospitalizations and make patients and families more confident in their ability to care for asthma. Written AAPs should be updated and reviewed at every health care service encounter (e.g. pharmacy, doctor visit, ED visit, or hospitalization). Various AAPs are usually available for free, so enough copies should be given to the patient to have at home, school, daycare, grandparents, among other places.

How to Use an AAP

By using the stoplight color scheme of green, yellow, and red, patients and families are informed about daily actions to maintain symptom control and to use interventions when needed for symptoms or exacerbations (Figure 9).

Green Means "Go"

In this zone, the patient has no symptoms, can go to school, can run and play, and sleeps well. Patients with persistent asthma still take daily medicines in this zone, and the medicines are listed in the AAP, complete with strength, dosage form, and dosing. An exercise-induced asthma regimen with a SABA as pretreatment is also listed in the AAP.

Yellow Means "Caution"

In this zone, symptoms of asthma or an exacerbation are starting (i.e. cough, wheeze, chest tightness), and the rescue-medicine regimen should be started. Patients should not stop any "green zone" medicines; rescue therapy is additional. Standby oral steroids may be listed in this zone as well.

Red Means "Stop" or "Danger"

In this zone, the rescue medicine does not work or last a full 4 hours, and the patient has retractions, nasal flaring, sputum production, and is fatigued. In this zone, more rescue medicine is given as instructed, and patients are taught to seek medical care immediately at the ED or UC or to call 9-1-1.

Other Components

Other information that must be included in a patient's AAP is the patient's name, the physician's name and office phone number, the severity of the asthma, and the patient-specific asthma triggers.

Do Not Reinvent the Wheel

If your practice or pharmacy site does not have an AAP, samples are available on the Internet. Sites such as those for the American Lung Association (Chicago, IL); National Heart, Lung, and Blood Institute (Bethesda, MD); or American Academy of Allergy Asthma & Immunology (Milwaukee, WI). The Centers for Disease Control and Prevention Web site (http://www.cdc.gov/asthma/tools_for_control.htm) has multiple

Asthma Action Plan

For: _____ Doctor: _____ Date: _____

Doctor's Phone Number _____ Hospital/Emergency Department Phone Number _____

GREEN ZONE

Doing Well

- No cough, wheeze, chest tightness, or shortness of breath during the day or night
- Can do usual activities

And, if a peak flow meter is used,

Peak flow: more than _____
(80 percent or more of my best peak flow)

My best peak flow is: _____

Take these long-term control medicines each day (include an anti-inflammatory).

Medicine	How much to take	When to take it
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____
Before exercise ❒ _____	❒ 2 or ❒ 4 puffs _____	5 minutes before exercise

YELLOW ZONE

Asthma Is Getting Worse

- Cough, wheeze, chest tightness, or shortness of breath, or
- Waking at night due to asthma, or
- Can do some, but not all, usual activities

-Or-

Peak flow: _____ to _____
(50 to 79 percent of my best peak flow)

First

Add: quick-relief medicine—and keep taking your GREEN ZONE medicine.

_____ (short-acting beta$_2$-agonist)
❒ 2 or ❒ 4 puffs, every 20 minutes for up to 1 hour
❒ Nebulizer, once

Second

If your symptoms (and peak flow, if used) return to GREEN ZONE after 1 hour of above treatment:
❒ Continue monitoring to be sure you stay in the green zone.

-Or-

If your symptoms (and peak flow, if used) do not return to GREEN ZONE after 1 hour of above treatment:
❒ Take: _____ (short-acting beta$_2$-agonist) ❒ 2 or ❒ 4 puffs or ❒ Nebulizer
❒ Add: _____ (oral steroid) mg per day For _____(3–10) days
❒ Call the doctor ❒ before/ ❒ within _____ hours after taking the oral steroid.

RED ZONE

Medical Alert!

- Very short of breath, or
- Quick-relief medicines have not helped, or
- Cannot do usual activities, or
- Symptoms are same or get worse after 24 hours in Yellow Zone

-Or-

Peak flow: less than _____
(50 percent of my best peak flow)

Take this medicine:

❒ _____ (short-acting beta$_2$-agonist) ❒ 4 or ❒ 6 puffs or ❒ Nebulizer

❒ _____ (oral steroid) mg

Then call your doctor NOW. Go to the hospital or call an ambulance if:
- You are still in the red zone after 15 minutes AND
- You have not reached your doctor.

DANGER SIGNS
- **Trouble walking and talking due to shortness of breath**
- **Lips or fingernails are blue**

- **Take ❒ 4 or ❒ 6 puffs of your quick-relief medicine AND**
- **Go to the hospital or call for an ambulance _____ (phone) NOW!**

See the reverse side for things you can do to avoid your asthma triggers.

Figure 9. Asthma Action Plan.

How To Control Things That Make Your Asthma Worse

This guide suggests things you can do to avoid your asthma triggers. Put a check next to the triggers that you know make your asthma worse and ask your doctor to help you find out if you have other triggers as well. Then decide with your doctor what steps you will take.

Allergens

❒ **Animal Dander**

Some people are allergic to the flakes of skin or dried saliva from animals with fur or feathers.

The best thing to do:

- Keep furred or feathered pets out of your home.

If you can't keep the pet outdoors, then:

- Keep the pet out of your bedroom and other sleeping areas at all times, and keep the door closed.
- Remove carpets and furniture covered with cloth from your home. If that is not possible, keep the pet away from fabric-covered furniture and carpets.

❒ **Dust Mites**

Many people with asthma are allergic to dust mites. Dust mites are tiny bugs that are found in every home—in mattresses, pillows, carpets, upholstered furniture, bedcovers, clothes, stuffed toys, and fabric or other fabric-covered items.

Things that can help:

- Encase your mattress in a special dust-proof cover.
- Encase your pillow in a special dust-proof cover or wash the pillow each week in hot water. Water must be hotter than 130° F to kill the mites. Cold or warm water used with detergent and bleach can also be effective.
- Wash the sheets and blankets on your bed each week in hot water.
- Reduce indoor humidity to below 60 percent (ideally between 30—50 percent). Dehumidifiers or central air conditioners can do this.
- Try not to sleep or lie on cloth-covered cushions.
- Remove carpets from your bedroom and those laid on concrete, if you can.
- Keep stuffed toys out of the bed or wash the toys weekly in hot water or cooler water with detergent and bleach.

❒ **Cockroaches**

Many people with asthma are allergic to the dried droppings and remains of cockroaches.

The best thing to do:

- Keep food and garbage in closed containers. Never leave food out.
- Use poison baits, powders, gels, or paste (for example, boric acid). You can also use traps.
- If a spray is used to kill roaches, stay out of the room until the odor goes away.

❒ **Indoor Mold**

- Fix leaky faucets, pipes, or other sources of water that have mold around them.
- Clean moldy surfaces with a cleaner that has bleach in it.

❒ **Pollen and Outdoor Mold**

What to do during your allergy season (when pollen or mold spore counts are high):

- Try to keep your windows closed.
- Stay indoors with windows closed from late morning to afternoon, if you can. Pollen and some mold spore counts are highest at that time.
- Ask your doctor whether you need to take or increase anti-inflammatory medicine before your allergy season starts.

Irritants

❒ **Tobacco Smoke**

- If you smoke, ask your doctor for ways to help you quit. Ask family members to quit smoking, too.
- Do not allow smoking in your home or car.

❒ **Smoke, Strong Odors, and Sprays**

- If possible, do not use a wood-burning stove, kerosene heater, or fireplace.
- Try to stay away from strong odors and sprays, such as perfume, talcum powder, hair spray, and paints.

Other things that bring on asthma symptoms in some people include:

❒ **Vacuum Cleaning**

- Try to get someone else to vacuum for you once or twice a week, if you can. Stay out of rooms while they are being vacuumed and for a short while afterward.
- If you vacuum, use a dust mask (from a hardware store), a double-layered or microfilter vacuum cleaner bag, or a vacuum cleaner with a HEPA filter.

❒ **Other Things That Can Make Asthma Worse**

- Sulfites in foods and beverages: Do not drink beer or wine or eat dried fruit, processed potatoes, or shrimp if they cause asthma symptoms.
- Cold air: Cover your nose and mouth with a scarf on cold or windy days.
- Other medicines: Tell your doctor about all the medicines you take. Include cold medicines, aspirin, vitamins and other supplements, and nonselective beta-blockers (including those in eye drops).

U.S. Department of Health and Human Services
National Institutes of Health

National Heart Lung and Blood Institute

For More Information, go to: www.nhlbi.nih.gov

NIH Publication No. 07-5251
April 2007

Figure 9. Asthma Action Plan (*cont.*).

links to AAPs that can be printed and completed or completed electronically. Many are also available in Spanish. For details on the US National Institutes of Health (NIH, Bethesda, MD) recommendations regarding the use of AAPs, refer to pages 115 to 120 of the guidelines at http://www.nhlbi.nih.gov/files/docs/guidelines/asthgdln.pdf.

CONCLUSION

Asthma is a complex, multifactorial disease requiring consistent education at all points of care. It is a chronic condition that is dynamic throughout a patient's life, changing in severity and the way it is managed by the patient and his or her health care team. A patient's asthma status may change from intermittent to persistent throughout his or her life. Albuterol is the drug of choice for relief of acute flares because it is effective and well tolerated by patients. The cornerstone of long-term maintenance therapy of asthma is ICS. In more-persistent classifications, other drug classes, such as LTRAs and LABAs, are added to ICS therapy. Pharmacists are in a unique position to educate patients on the differences among commonly used asthma medications, to teach patients appropriate asthma device techniques and cleaning, and to understand how to refer to the AAP for daily instruction. This information should be used to assess appropriate medication use and to provide self-management education to patients and their caregivers.

Disclosure The authors declare no conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria. The authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Abbreviations AAA, applied to affected area; AAP, asthma action plan; ACQ, asthma control questionnaire; ACT, asthma control test; ATAQ, asthma therapy assessment questionnaire; BID, twice daily; CC, chief complaint; DPI, dry-powdered inhalers; ED, emergency department; EIB, exercised-induced bronchoconstriction; FDA, US Food and Drug Administration; FHx, family history; HFA, hydrofluoroalkane; HPI, history of present illness; ICS, inhaled corticosteroids; LABA, long-acting β-agonists; LT, leukotriene; LTRA, leukotriene receptor antagonists; MDI, metered dose inhaler; NHIS, National Health Interview Survey; NHLBI, National Heart, Lung, and Blood Institute; NIH, National Institutes of Health; PFM, peak flow monitoring; PFT, pulmonary function test; PMH, past medical history; po, by mouth; prn, as needed; q, every; SABA, short-acting β-agonist; UC, urgent care; VHC, valved holding chamber

Correspondence Barnabas M. John, PharmD, University of Oklahoma, College of Pharmacy, 4502 E 41st Street, Suite 2H25, Tulsa, OK 74135, email: bmjohn@saintfrancis.com

REFERENCES

1. National Asthma Education and Prevention Program. *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma.* Bethesda, MD: National Institutes of Health, 2007; NIH publication 07-4051.
2. National Center for Health Statistics. *Current Asthma Prevalence Percents by Age, United States: National Health Interview Survey*, Atlanta, GA: Centers for Disease Control and Prevention; 2012:table 4-1.
3. National Center for Health Statistics. *Asthma Attack Prevalence Percents Among Those With Current Asthma by Age, United States: National Health Interview Survey*. Atlanta, GA: Centers for Disease Control and Prevention; 2012:table 6-1.
4. Centers for Disease Control and Prevention. *Asthma Facts CDC's National Asthma Control Program Grantees*. Atlanta, GA: US Department of Health and Human Services; 2013.
5. Weiss ST, Speizer FE. Epidemiology and natural history. In: Weiss EB, Stein M, eds. *Bronchial Asthma Mechanisms and Therapeutics*. 3rd ed. Toronto, ON, Canada: Little Brown; 1993:15-25.
6. Busse WW, Lemanske RF Jr. Asthma. *N Engl J Med.* 2001;344(5):350-362.
7. del Giudice MM, Pezzulo A, Capristo C, et al. Leukotriene modifiers in the treatment of asthma in children. *Ther Adv Respir Dis.* 2009;3(5):245-251.
8. Lexicomp Online. *Pediatric & Neonatal Lexi-Drugs*, Hudson, OH: Lexi-Comp, Inc; http://webstore.lexi.com/Pediatric-Lexi-Drugs. Accessed March 29, 2014.
9. Walters EH, Walters J. Inhaled short acting β2-agonist use in chronic asthma: regular versus as needed treatment. *Cochrane Database Syst Rev*. 2003;(2):CD001285.
10. Sunovion Pharmaceuticals. Xopenex (R) (Levalbuterol Inhalation Solution) [package insert]. Marlborough, MA: Sunovion Pharmaceuticals Inc; September 2012.

11. D'Alonzo GE Jr. Levalbuterol in the treatment of patients with asthma and chronic obstructive lung disease. *J Am Osteopath Assoc.* 2004;104(7):288-293.
12. Jat KR, Khairwa A. Levalbuterol versus albuterol for acute asthma: a systematic review and meta-analysis. *Pulm Pharmacol Ther*. 2013;26(2):239-248.
13. Scott VL, Frazee LA. Retrospective comparison of nebulized levalbuterol and albuterol for adverse events in patients with acute airflow obstruction. *Am J Ther.* 2003;10(5):341-347.
14. Carl JC, Myers TR, Kirchner HL, Kercsmar CM. Comparison of racemic albuterol and levalbuterol for treatment of acute asthma. *J Pediatr.* 2003;143(6):731-736.
15. Laitinen LA, Laitinen A, Haahtela T. A comparative study of the effects of an inhaled corticosteroid, budesonide, and a β2-agonist, terbutaline, on airway inflammation in newly diagnosed asthma: a randomized, double-blind, parallel-group controlled trial. *J Allergy Clin Immunol Pract.* 1992;90(1):32-42.
16. Oborne J, Mortimer K, Hubbard RB, et al. Quadrupling the dose of inhaled corticosteroid to prevent asthma exacerbations: a randomized, double-blind, placebo-controlled, parallel-group clinical trial. *Am J Respir Crit Care Med.* 2009;180(7): 598-602.
17. Dinakar C, Oppenheimer J, Portnoy J, et al. Management of acute loss of asthma control in the yellow zone: a practice parameter. *Ann Allergy Asthma Immunol*. 2014;113(2):143-159.
18. Kelly HW, Sternberg AL, Lescher R, et al; CAMP Research Group. Effect of inhaled glucocorticoids in childhood on adult height. *N Engl J Med.* 2012;367(10):904-912.
19. Scarfone RJ. Acute asthma exacerbations in children: outpatient management. http://www.uptodate.com/contents/acute-asthma-exacerbations-in-children-outpatient-management?source=search_result&search=oral+steroids+for+asthma&selectedTitle=2%7E150#H24. Accessed July 19, 2016.
20. Greenberg RA, Kerby G, Roosevelt GE. A comparison of oral dexamethasone with oral prednisone in pediatric asthma exacerbations treated in the emergency department. *Clin Pediatr (Phila).* 2008;47(8):817-823.
21. Grzelewski T, Stelmach I. Exercise-induced bronchoconstriction in asthmatic children: a comparative systematic review of the available treatment options. *Drugs*. 2009;69(12):1533-1553.
22. US Food and Drug Administration. Long-acting beta-agonist (LABAs): new safe use requirements. http://www.fda.gov/safety/medwatch/safetyinformation/safetyalertsforhumanmedicalproducts/ucm201003.htm. Accessed July 19, 2016.
23. van der Molen T, Postma DS, Turner MO, et al. Effects of the long acting beta agonist formoterol on asthma control in asthmatic patients using inhaled corticosteroids: the Netherlands and Canadian Formoterol Study investigators. *Thorax.* 1997;52(6):535-539.
24. Dumitru C, Chan SM, Turcanu V. Role of leukotriene receptor antagonists in the management of pediatric asthma: an update. *Paediatr Drugs.* 2012;14(5):317-330.
25. Montuschi P, Peters-Golden ML. Leukotriene modifiers for asthma treatment. *Clin Exp Allergy.* 2010;40(12):1732-1741.
26. Matsuse H, Kohno S. Leukotriene receptor antagonists pranlukast and montelukast for treating asthma. *Expert Opin Pharmacother.* 2014;15(3):353-363.
27. Schumock GT, Stayner LT, Valuck RJ, et al. Risk of suicide attempt in asthmatic children and young adults prescribed leukotriene-modifying agents: a nested case-control study. *J Allergy Clin Immunol.* 2012;130(2):368-375.
28. Philip G, Hustad C, Noonan G, et al. Reports of suicidality in clinical trials of montelukast. *J Allergy Clin Immunol.* 2009;124(4):691-696 e6.
29. Philip G, Hustad CM, Malice MP, et al. Analysis of behavior-related adverse experiences in clinical trials of montelukast [published correction in *J Allergy Clin Immunol*. 2010;125(5):1019]. *J Allergy Clin Immunol*. 2009;124(4):699-706.e8.
30. Moore TJ, Furberg CD, Mattison DR, et al. (2014) QuarterWatch: special report on children: adverse drug events in children under age 18. Horsham, PA: Institute for Safe Medication Practices. URL:http://www.ismp.org/quarterwatch/pdfs/2013Q1-Kids-Special.pdf. Accessed July 19, 2016.

31. Hess DR. Aerosol delivery devices in the treatment of asthma. *Respir Care.* 2008;53(6):699-723.
32. Berger W. Aerosol devices and asthma therapy. *Curr Drug Deliv*. 2009;6(1):38-49.
33. Adachi YS1, Adachi Y, Itazawa T et al. Ability of preschool children to use dry powder inhalers as evaluated by In-Check Meter. *Pediatr Int*. 2006;48(1):62-65.
34. Rubin BK. Bye-bye, blow-by. *Respir Care*. 2007;52(8):981.
35. Murakami G, Igarashi T, Adachi Y, et al. Measurement of bronchial hyperreactivity in infants and preschool children using a new method. *Ann Allergy* 1990;64(4):383-387.
36. Dolovich MB, Ahrens RC, Hess DR, et al; College of Chest Physicians; American College of Asthma, Allergy, and Immunology. Device selection and outcomes of aerosol therapy: evidence-based guidelines: American College of Chest Physicians/American College of Asthma, Allergy, and Immunology. *Chest.* 2005;127(1):335-371.
37. US National Library of Medicine. DailyMed. Bethesda, MD: US NLIM. http://dailymed.nlm.nih.gov/dailymed/index.cfm. Accessed July 19, 2016.
38. Kliegman RM, Stanton BF, St. Gemell JW, et al, eds. *Nelson Textbook of Pediatrics*. 19th ed. Philadelphia, PA: Saunders Elsevier; 2011.
39. Wildhaber JH, Dore ND, Wilson JM, et al. Inhalation therapy in asthma: nebulizer or pressurized metered-dose inhaler with holding chamber? In vivo comparison of lung deposition in children. *J Pediatr.* 1999;135(1):28-33.

Answers:

1. Severity table (Figure 1). Rationale: the patient is not currently on a controller medication.
2. Severity is classified as *moderate persistent*. Rationale: The "daytime symptoms" and "B-agonist use" answers are in the "mild persistent" column. The number of exacerbations the patient had had in the previous year puts her in the persistent asthma category (there is no specific recommendation detailing how many would place a patient in 1 of the 3 persistent categories). The highest-rated component, "nighttime symptoms," is in the "moderate persistent" column. The highest-rated component determines the severity rating, so this patient's severity would be classified as moderate persistent. Only when lung function test information is available is it used to rate the patient's asthma severity.
3. Addition of a medium-dose ICS to the SABA prn. Rationale: The patient would be at "step 3" in which low-dose (ICS) + LABA or a medium-dose of ICS would be initiated. Notice that ICS is the preferred controller therapy, and other agents are added as indicated. An alternative therapy is low-dose ICS plus a LTRA (e.g. montelukast). This regimen could be used in a patient with comorbid allergic rhinitis or if the family was resistant to increasing doses of inhaled steroids. If a patient has asthma only, an ICS + LABA treatment is an acceptable choice, as well, because the addition of LABAs improves asthma control, and a combination product in 1 device may improve likelihood of adherence. A clinician using Figure 8 in this document, along with patient age and recommended steroid dose level, can determine ICS options and corresponding total daily dose. This patient would be given an AAP and would be treated for approximately 3 months if therapy was effective and well tolerated.
4. At each opportunity, health care providers must reassess adherence, inhaler technique, environmental control, and comorbid conditions. Because this patient recently started a new medicine, an ICS, poor adherence was possible because of confusion among the different medicines used to treat asthma. A common reason patients are non-adherent is that they have confused their controller and rescue medications or perceive their rescue medication is more effective than the controller medication. A benign question to ask to assess about adherence or confusion is "What is the color (or name) of the medication used every day to control your asthma?" Poor technique or not using a VHC (with or without a facemask) is an additional reason patients may be poorly controlled despite starting an ICS. This is best assessed by having the patient demonstrate their technique.

This is a Continuing Pharmacy Education (CPE) article.

To receive continuing education credit, you must pass a post-test. To register for CE and to access the post-test, please direct your browser to: http://tinyurl.com/jpptce

Program Title: Asthma Review for Pharmacists Providing Asthma Education
Program Number: 0180-0000-16-500-H01-P
Program Type: Knowledge-based
Program Hours: 1 contact hour (0.1 CEU's)

Upon completion of this program, the practitioner will be able to

1. Identify asthma severity, control, and step therapy using the current 2007 NHLBI guideline tables.
2. Describe how commonly used asthma medications affect asthma pathophysiology.
3. Explain to a patient and caregiver the proper use of the following medication classes in asthma care: quick relievers, ICSs, oral steroids, LABAs, and LTRAs.
4. Explain to a patient and caregiver at least 3 side effects or concerns with common medications used in asthma care.
5. Teach a patient and caregiver to properly use and clean an MDI, VHC or spacer, and nebulizer according to manufacturer specifications.
6. Create an AAA, according to 2007 NHLBI guidelines, which includes appropriate controller(s), rescue medication, symptoms, and patient-specific triggers.

PPAG is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. For more information, go to: https://www.ppag.org/index.cfm?pg=Accreditation

Continuing Education Assessment Questions

1. A 7-year-old patient with an acute asthma exacerbation was on fluticasone and albuterol for 2 years but stopped 6 months ago. Which of the following figures is the appropriate one to address his or her asthma at a current visit?
   a. Classifying severity and initiating treatment in children 5–11 years old.
   b. Assessing asthma control and adjusting therapy in children 5–11 years old.
   c. Classifying severity and initiating treatment in children 12 years and older.
   d. Assessing asthma control and adjusting therapy in children 12 years and older.

2. An 8-year-old patient who is not currently using a controller medication is started on prednisolone liquid for an acute asthma exacerbation.

   Impairment
   Symptoms once daily with exercise (until this week, when it became worse)
   Night symptoms 4 nights/wk (until this week, when it became worse)
   Uses 2 puffs albuterol with VHC BID (until this week, when it was used up to q 2 hr)
   Some activity limitation (which became severe this week)

   Risk
   This is the second course of oral steroids in the past year
   What is this patient's asthma severity?

   a. Intermittent asthma
   b. Mild persistent asthma
   c. Moderate persistent asthma
   d. Severe persistent asthma

3. For the patient in question 2, which controller therapy should be started?
   a. None is required
   b. Low-dose ICS
   c. Medium-dose ICS
   d. High-dose ICS

4. Which of the following would decrease airway inflammation associated with asthma?
   a. Albuterol
   b. Salmeterol
   c. Ipratropium
   d. Budesonide

5. When using albuterol every 4 hours as needed for shortness of breath in a 10-year-old with asthma, which of the following is the best option?
   a. Albuterol 1.25 mg use 1 vial every 4 hours as needed for shortness of breath
   b. Albuterol 2 puff with VHC every 4 hours as needed for shortness of breath
   c. Albuterol 4 puffs with VHC every 4 hours as needed for shortness of breath
   d. Albuterol 4 puffs every 4 hours as needed for shortness of breath

6. When compared with albuterol, levalbuterol is statistically superior because it
   a. Improves respiratory rate
   b. Increases oxygen saturations
   c. Reduces hospital admission rate
   d. Decreases duration of ED care

7. Rinsing the mouth after using a VHC to administer ICS decreases the chance of getting the following side effects EXCEPT
   a. Decreased final adult height
   b. Dysphonia
   c. Thrush
   d. Sore throat

8. When counseling on the use of ICS for patients with asthma, which of the following is accurate?
   a. Maximum effects occur within 1 week.
   b. It is appropriate to use ICS to treat acute asthma flares.
   c. ICS is a cure for a patient's asthma.
   d. Maximum effect takes 2 weeks to occur.

9. Which of the following is TRUE for inhaled asthma medications?
   a. Anticholinergic rescue medications are as effective as SABAs.
   b. LABAs have a role as monotherapy for some persistent asthmatics.
   c. Doubling an ICS should be recommended to manage an asthma flare at home.
   d. Use of a SABA more than twice per week (not including before exercise) indicates poorly controlled asthma.

10. Which of the following is true regarding administration of short courses of oral steroids (i.e. prednisone or prednisolone) for the treatment of asthma flares?
    a. Can be substituted with increased doses of inhaled steroids.
    b. Are typically 5 days long without a taper.
    c. Do not indicate the level of risk for a patient with asthma.
    d. Have no effect on the rates of hospitalization from asthma flares.

11. Which of the following is true regarding dexamethasone for acute asthma exacerbations?
    a. It causes more nausea and vomiting than prednisolone.
    b. It is comparable to prednisolone in treating severe asthma exacerbations.
    c. 1 or 2 doses work as well as 5 days of prednisolone in terms of lowered rates of unscheduled doctor visits for asthma, hospital admission rates, and vomiting.
    d. The liquid form is more palatable than prednisolone sodium phosphate.

12. The role of LTRAs in asthma therapy include
    a. Initial controller monotherapy
    b. Second-line, add-on controller therapy
    c. Third-line, add-on controller therapy
    d. B and C

13. Which of the following is true about montelukast?
    a. May be effective in treating exercise-induced bronchoconstriction
    b. Frequently causes neuropsychiatric side effects, such as agitation and suicidal ideations
    c. May be effective in patients with asthma and allergic rhinitis
    d. Only A and C

14. Which step is NOT correct when administering an MDI with VHC and mouthpiece?
    a. Take off cap, shake inhaler for 10 seconds, and place in VHC.
    b. Press down on the inhaler once and inhale slowly for a count of 10.
    c. Administer 2 puffs of the inhaler into the VHC and breathe in slowly.
    d. Hold breath 10 seconds, wait 1 minute, then repeat the entire process, if indicated.

15. Which step is NOT correct when administering an MDI with VHC and face mask
    a. Take off cap, shake inhaler for 10 seconds, and place in holding chamber.
    b. Place mask over the nose and mouth.
    c. Hold breath 10 seconds, wait 1 minute, then repeat the entire process, if indicated.
    d. Press down on the inhaler once and breathe in and out 6 times.

16. At which age can most children start to produce the appropriate, forceful inhalation for proper administration of a DPI?
    a. 4 years old
    b. 5 years old
    c. 6 years old
    d. 7 years old

17. Which of the following is an advantage of aerosol medication administration?
    a. Technique is easier to teach.
    b. The duration of medication administration is faster than any other delivery device.
    c. Medication administered via nebulizer is more effective than that delivered by MDI with VHC and facemask.
    d. Children who do not like facemasks or holding a delivery device can be given the medication using blow-by technique.

18. What is the recommendation for how frequently VHCs should be cleaned?
    a. Every 3 days
    b. Every week
    c. Every other week
    d. Once a month

19. Which part of the aerosol delivery device should not be washed with liquid dish soap and water?
    a. Tubing
    b. Facemask
    c. Nebulizer
    d. Mouth piece

20. For an AAP to be effective
    a. It should incorporate a patient's daily signs and symptoms along with peak flow meter readings.
    b. It should be discussed between the patient caregiver and health care provider at every encounter when asthma is discussed.
    c. A practitioner must use one that is available in electronic format.
    d. It can be helpful without extraneous information, such as emergency contact and triggers.