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Asthma Diagnosis and Treatment Guideline

Last guideline approval: July 2015

Guidelines are systematically developed statements to assist patients and providers in choosing appropriate health care for specific clinical conditions. While guidelines are useful aids to assist providers in determining appropriate practices for many patients with specific clinical problems or prevention issues, guidelines are not meant to replace the clinical judgment of the individual provider or establish a standard of care. The recommendations contained in the guidelines may not be appropriate for use in all circumstances. The inclusion of a recommendation in a guideline does not imply coverage. A decision to adopt any particular recommendation must be made by the provider in light of the circumstances presented by the individual patient.

Definition

Asthma is a chronic inflammatory disorder of the airways. It is defined by the history of respiratory symptoms such as wheezing, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation (GINA 2014).

Diagnosis

Asthma is a diagnosis of exclusion. It is important to consider the pattern of symptoms and triggers and to rule out conditions that cause wheezing, coughing, and dyspnea before making the diagnosis.

The evidence for the diagnosis of asthma should be documented before starting controller treatment, as it is often more difficult to confirm a diagnosis afterwards.

To establish a diagnosis of asthma:

1. **Use history and physical** to determine whether symptoms of recurrent episodes of airflow obstruction or airway hyper-responsiveness are present.

   Symptoms include:
   - Wheezing (polyphonic, musical or whistling sounds, predominantly expiratory)
   - Cough
   - Chest tightness
   - Dyspnea
   - Worsening of symptoms at night or in the presence of environmental stimuli

2. **Use spirometry** in patients 5 years and older to determine whether airflow obstruction is at least partially reversible after use of a bronchodilator. In patients of all ages, reversibility is indicated by an increase of at least 12% in FEV_1 from baseline. In adults, an increase in FEV_1 of greater than 200 mL from baseline also constitutes reversibility. Note that having normal lung function does not exclude the diagnosis of asthma, especially in children.

   A note about spirometry
   Spirometry provides an objective measurement of asthma severity and response to therapy, and can be useful in assessing patients who may under-report or over-report their symptoms.

   Spirometry should be considered when:
   - Considering an initial diagnosis of asthma (or as part of differential diagnosis)
   - Assessing response to treatment after a change in medication
   - Assessing asthma control in patients with persistent asthma

3. **Exclude alternative diagnoses** such as pulmonary diseases (e.g., COPD, pulmonary fibrosis, bronchiectasis), upper airway conditions (e.g., chronic allergic rhinitis and sinusitis, vocal cord dysfunction, obstructive sleep apnea), congestive heart failure, and other causes (e.g., foreign body in trachea or bronchus, GERD, enlarged lymph nodes or tumors, cystic fibrosis, drug-related cough).

Classify Current Severity

Asthma severity (see Table 1) is used to guide treatment decisions in patients with either a new or a past diagnosis of asthma who are not currently on medication. (For patients currently taking medications, see “Assess Control,” pp. 4–6.) Severity is easiest to assess at the initial diagnosis, before patients are taking long-term control medications, but it can also be measured once asthma control is achieved by

determining the amount of medication needed for control. Severity is classified as intermittent or persistent (mild, moderate or severe).

Note: Because **children under age 5** are more likely to have wheezing episodes than older children or adults, asthma is more difficult to diagnose in this age group. At times reactive airway disease (RAD) in young children will remit around 5 years of age. However, some of these patients will continue to have symptoms. Children under 5 years of age who have RAD and also certain risk factors (sensitization to foods and/or inhaled allergens, atopic dermatitis, wheezing apart from colds, and parental history of asthma) are more likely to have continued symptoms after 5 years of age and are more likely to respond to inhaled corticosteroids (ICS).

Classify asthma severity: patients of all ages

Table 1. Classifying asthma severity in patients NOT currently taking medications (includes recently diagnosed patients and those with a past diagnosis not currently on medication)
The result is based on the most severe category of impairment or risk.

Impairment (Over last 2–4 weeks)	**Intermittent asthma**	**Persistent asthma**		
		Mild	**Moderate**	**Severe**
Symptoms	≤ 2 days/week	≥ 3 days/week but not daily	Daily	Throughout day
Nighttime awakenings				
Age ≥ 5 years	≤ 2 nights/month	3–4 nights/month	> 1 night/week but not nightly	Often 7 nights/week
Age < 5 years	None	1–2 nights/month	3–4 nights/month	> 1 night/week
Short-acting $beta_2$-agonist use (for rescue, not exercise prophylaxis)	≤ 2 days/week [1]	≥ 3 days/week but ≤ 1x/day	Daily	Several times a day
Interference with normal activity	None	Minor limitation	Some limitation	Extreme limitation
Lung function				
FEV_1 predicted or personal best	Normal [2] between exacerbations; > 80%	> 80%	60–80%	< 60%
FEV_1 /FVC				
Age ≥ 12 years	Normal [2]	Normal [2]	Reduced 5%	Reduced > 5%
Age 5–11 years	> 85%	> 80%	75–80%	< 75%
Risk (Over last year)	**Intermittent asthma**	**Persistent asthma**		
Exacerbations requiring systemic corticosteroids	≤ 1x/year	≥ 2x/year		

[1] ≤ 2 days/week of short-acting $beta_2$-agonist for rescue means ≤ 2 doses (4 puffs) per week.
[2] Normal FEV_1 /FVC by age group (not assessed in children age < 5 years):
8–19 years = 0.85
20–39 years = 0.80
40–59 years = 0.75
60–80 years = 0.70

Assess Control

Asthma control is the degree to which asthma symptoms are minimized in patients with an established diagnosis of asthma. The degree of control is used to determine whether a patient's medications should be adjusted. Control is classified as well controlled, not well controlled, and very poorly controlled.

Both asthma severity and control are evaluated by the degree of **impairment** (the frequency and intensity of symptoms and functional limitations) that the patient is experiencing and by the **risk** of asthma exacerbation, progressive decline in lung function, or treatment-related adverse effects.

Patients aged < 5 years

Table 2. Patients aged < 5 years *currently taking* medications: asthma control assessment and treatment recommendations
Assess each component over the last 2–4 weeks. The result is based on the score of the most severe component. The treatment recommendation is determined by the level of asthma control. See Table 6 (p. 9) for specific pharmacologic recommendations based on this step-wise approach.

	Asthma is:		
Clinical assessment	***Well controlled***	***Not well controlled***	***Very poorly controlled***
Symptoms	≤ 2 days/week	> 2 days/week	Throughout day
Nighttime awakenings	≤ 1x/month	> 1x/month	> 1x/week
Short-acting beta$_2$ agonist use (for rescue, not exercise prophylaxis)	≤ 2 days/week [1]	> 2 days/week [1]	Several times a day
Interference with normal activity	None	Some limitation	Extreme limitation
Exacerbations requiring systemic corticosteroids	≤ 1x/year	2–3x/year	> 3x/year
Treatment recommendation *Note:* Before stepping up therapy, review the patient's adherence to medication, inhaler technique, and environmental control, and consider alternative diagnoses.	***Well controlled***	***Not well controlled***	***Very poorly controlled***
	Maintain therapy at current step. If well controlled for 3 months or longer, consider step down.	Step up 1 step.	Step up 1–2 steps. Consider short course of systemic corticosteroids.
Follow-up See "Follow-up/Monitoring" (p. 12) for more information.	1–6 months	2–6 weeks	2 weeks

[1] ≤ 2 days/week of short-acting beta$_2$-agonist for rescue means ≤ 2 doses (4 puffs) per week, and > 2 days/week means > 2 doses (4 puffs) per week.

Patients aged 5–11 years

Table 3. Patients aged 5–11 years *currently taking* medications: asthma control assessment and treatment recommendations
Assess each component over the last 2–4 weeks. The result is based on the score of the most severe component. The treatment recommendation is determined by the level of asthma control. See Table 6 (p. 9) for specific pharmacologic recommendations based on this step-wise approach.

	Asthma is:		
Clinical assessment	***Well controlled***	***Not well controlled***	***Very poorly controlled***
Symptoms	≤ 2 days/week	> 2 days/week	Throughout the day
Nighttime awakenings	≤ 1x/month	≥ 2x/month	≥ 2x/week
Short-acting beta$_2$-agonist use (for rescue, not exercise prophylaxis)	≤ 2 days/week [1]	> 2 days/week [1]	Several times a day
Interference with normal activity	None	Some limitation	Extreme limitation
Exacerbations requiring systemic corticosteroids	≤ 1x/year	2–3x/year	> 3x/year
Childhood Asthma Control Test (ACT) questionnaire Consider use as an adjunct objective measure to the clinical assessment. Must be confirmed by follow-up discussion.			
ACT score	≥ 20	13–19	≤ 12
The ACT questionnaire is available as a flow sheet in Epic (see the Pharmacy job aid) and in a paper version through the Print Shop.			
Lung function (spirometry) Consider use as an adjunct objective measure to the clinical assessment in patients who have poor response to treatment.			
FEV$_1$ predicted	> 80%	60–80%	< 60%
FEV$_1$ /FVC	> 0.80	0.75–0.80	< 0.75
Treatment recommendation	***Well controlled***	***Not well controlled***	***Very poorly controlled***
Note: Before stepping up therapy, review the patient's adherence to medication, inhaler technique, and environmental control, and consider alternative diagnoses.	Maintain therapy at current step. If well controlled for 3 months or longer, consider step down.	Step up at least 1 step.	Step up 1–2 steps. Consider short course of systemic corticosteroids.
Follow-up See "Follow-up/Monitoring" (p. 12) for more information.	1–6 months	2–6 weeks	2 weeks

[1] ≤ 2 days/week of short-acting beta$_2$-agonist for rescue means ≤ 2 doses (4 puffs) per week, and > 2 days/week means > 2 doses (4 puffs) per week.

Patients aged ≥ 12 years

Table 4. Patients aged ≥ 12 years *currently taking* medications: asthma control assessment and treatment recommendations
Assess each component over the last 2–4 weeks. The result is based on the score of the most severe component. The treatment recommendation is determined by the level of asthma control. See Table 6 (p. 9) for specific pharmacologic recommendations based on this step-wise approach.

	Asthma is:		
Clinical assessment	***Well controlled***	***Not well controlled***	***Very poorly controlled***
Symptoms	≤ 2 days/week	> 2 days/week	Throughout the day
Nighttime awakenings	≤ 2x/month	1–3x/week	≥ 4x/week
Short-acting beta$_2$-agonist use (for rescue, not exercise prophylaxis)	≤ 2 days/week [1]	> 2 days/week [1]	Several times a day
Interference with normal activity	None	Some limitation	Extreme limitation
Exacerbations requiring systemic corticosteroids	≤ 1x/year	≥ 2x/year	≥ 2x/year
Adult Asthma Control Test (ACT) questionnaire Consider use as an adjunct objective measure to the clinical history. Must be confirmed by follow-up discussion.			
ACT score	≥ 20	16–19	≤ 15
The ACT questionnaire is available as a flow sheet in Epic (see the Pharmacy job aid) and in a paper version through the Print Shop. *Note:* ACT question 4 is asking about how often short-acting beta$_2$-agonists are used for **rescue,** not for exercise prophylaxis.			
Lung function (spirometry) Consider use as an adjunct objective measure to the clinical assessment in patients who have poor response to treatment.			
FEV$_1$ predicted or personal best	> 80%	60–80%	< 60%
Treatment recommendation *Note:* Before stepping up therapy, review the patient's adherence to medication, inhaler technique, and environmental control, and consider alternative diagnoses.	***Well controlled***	***Not well controlled***	***Very poorly controlled***
	Maintain therapy at current step. If well controlled for 3 months or longer, consider step down.	Step up at least 1 step.	Step up 1–2 steps. Consider short course of systemic corticosteroids.
Follow-up See "Follow-up/Monitoring" (p. 12) for more information.	1–6 months	2–6 weeks	2 weeks

[1] ≤ 2 days/week of short-acting beta$_2$-agonist for rescue means ≤ 2 doses (4 puffs) per week, and > 2 days/week means > 2 doses (4 puffs) per week.

Treatment Goals

The goals of asthma treatment are to achieve good symptom control, maintain normal activity levels, minimize future risk of exacerbations, and reduce adverse effects from medications. It is also important to include the patient's own goals as these may be different from the medical goals. One way to think of treatment goals for children (and adults for the most part) is ensuring that the patient can "sleep, learn, and play" without limitations due to asthma. Effective asthma management requires partnership between the patient (or parent) and the health care provider.

Non-Pharmacologic Interventions

1. Provide asthma education

- Basic facts about asthma
- How medication works
- Importance of taking daily controller medication
- Inhaler technique
- Environmental control measures
- Use of written action plan (symptom- and/or peak flow–based)
- Need for regular follow-up visits

2. Encourage patient self-management

- **Self-monitor symptoms**. Patient monitors symptoms and/or uses a peak flow meter to assess control and signs of worsening. Consider use of a peak flow meter for patients who have moderate or severe persistent asthma or a history of severe exacerbations, or who poorly perceive airflow obstruction and worsening asthma. Patient instructions for using peak flow meters are available on ghc.org, at https://provider.ghc.org/open/caringForOurMembers/patientHealthEducation/conditionsDiseases/peakFlowMeter.pdf
- Follow an **Asthma Action Plan** (available as .AVSASTHMAACTIONPLAN in Epic and as a pamphlet on ghc.org, at https://provider.ghc.org/open/caringForOurMembers/patientHealthEducation/conditionsDiseases/asthmaPlan.pdf). With the provider, the patient develops and follows a written Asthma Action Plan that includes: instructions for daily management, self-monitoring to assess control and signs of worsening (either through symptoms or peak flow), and instructions for managing worsening asthma. Consider handing out the ACT questionnaire to parents and patients to identify when their asthma might not be well controlled.
- **Take medication correctly.** Patient instructions for using inhalers and devices are available on ghc.org, at https://provider.ghc.org/open/caringForOurMembers/patientHealthEducation/index.jhtml (Under "Conditions, Diseases, & Symptoms," see "Asthma.")
- **Limit or control environmental factors** that trigger or worsen symptoms, including: tobacco smoke, strong odors or sprays, dust mites, cockroaches, animal dander, pollen, outdoor mold, and indoor mold. Consider referral to Allergy & Asthma for testing to verify allergen sensitization and for specific advice on allergen avoidance.

3. Promote lifestyle interventions

- Encourage **physical activity**. Exercise has significant health benefits; exercise-induced asthma symptoms can be controlled, and engagement in regular exercise is encouraged.
- Encourage **tobacco cessation.** See the Tobacco Use Guideline for recommendations.
- Encourage **weight management.** See the Weight Management guidelines (Adult or Child/Adolescent) for recommendations.

4. Treat comorbid conditions that worsen asthma

- Allergic bronchopulmonary aspergillosis

- Environmental allergies
- GERD
- Obesity
- Obstructive sleep apnea
- Rhinitis
- Sinusitis
- Stress or depression
- Smoking

Pharmacologic Options

Medications for asthma are categorized into two general classes:

- Quick-relief medications to treat acute symptoms and exacerbations.
- Long-term control medications used daily to achieve and maintain control of persistent asthma.

Long-term controller medications are the mainstay in therapy for persistent asthma. Use of these medications reduces risk of emergency room visits and decreases overuse of rescue medications (albuterol).

The Asthma Medication Ratio HEDIS® measure is in place to encourage the use of controller medications for persistent asthma.

Asthma Medication Ratio (AMR) HEDIS measure
The percentage of members 5–85 years of age who were identified as having persistent asthma and had a ratio of controller medications to total asthma medications of 0.50 or greater during the measurement year.

In order to discourage overuse, consider ordering albuterol with no refills. This “one and done” approach has been shown to greatly reduce albuterol overuse in asthma patients. In Epic, the default for albuterol ***asthma*** is 0 refills. For albuterol ***COPD*** the default remains 11 refills.

Stepwise approach to initiating asthma treatment

A stepwise approach to therapy is recommended, based on asthma severity.

Table 5. Recommended step for initiating treatment based on asthma severity
See Table 6 for recommended drug regimens by age group.

Population	Intermittent asthma	Persistent asthma		
		Mild	Moderate	Severe
Age < 5 years	Step 1	Step 2	Step 3 [1]	Step 3 [1] or refer to Allergy & Asthma
Age 5–11 years	Step 1	Step 2	Step 3 [1,2]	Step 3 [1,2] or Step 4 or refer to Allergy & Asthma
Age ≥ 12 years	Step 1	Step 2	Step 3 [1]	Step 4 [1] or refer to Allergy & Asthma

[1] Consider short course of systemic corticosteroids.
[2] Using medium-dose inhaled corticosteroid option.

Stepwise approach to long-term asthma control

Table 6. Stepwise approach to long-term asthma control

Step #	Age < 5 years *Note:* The medications below may not be appropriate for all patients in this age range. See footnotes for details.	Age 5–11 years	Age ≥ 12 years
Step 1	**All ages: SABA** – albuterol. Quick-relief medication as needed.		
Step 2	**ICS low dose** 1st line: Fluticasone [1] 2nd line: Budesonide [2]	*Preferred* **ICS low dose** 1st line: Fluticasone 2nd line: Beclomethasone	*Preferred* **ICS low dose** 1st line: Beclomethasone 2nd line: Mometasone
	Alternative LTRA – montelukast	*Alternative* LTRA – montelukast	*Alternative* LTRA – montelukast
Step 3	**ICS medium dose** 1st line: Fluticasone [1] 2nd line: Budesonide [2]	*Preferred* **ICS medium dose** 1st line: Fluticasone 2nd line: Beclomethasone	*Preferred* **ICS medium dose** 1st line: Beclomethasone 2nd line: Mometasone
		Alternative ICS medium dose 1st line: Fluticasone 2nd line: Beclomethasone *and either* LABA – salmeterol *or* LTRA – montelukast	*Alternative* ICS/LABA low dose – fluticasone/salmeterol *or* ICS low dose 1st line: Beclomethasone 2nd line: Mometasone *and* LTRA – montelukast
Step 4	**ICS medium dose** 1st line: Fluticasone [1] 2nd line: Budesonide [2] ***and either*** **LTRA** – montelukast [3] *or* **LABA –** salmeterol [4]	*Preferred* **ICS/LABA medium dose** – fluticasone/salmeterol	*Preferred* **ICS/LABA medium dose –** fluticasone/salmeterol
		Alternative ICS medium dose 1st line: Fluticasone 2nd line: Beclomethasone *and* LTRA – montelukast	*Alternative* ICS medium dose 1st line: Beclomethasone 2nd line: Mometasone *and* LTRA – montelukast

[1] **Fluticasone** use is recommended by NHLBI and GINA for children of any age; however, fluticasone use is not FDA-approved for children under 4 years of age.
[2] Do not use **budesonide** in children under 12 months of age.
[3] Do not use **montelukast** for asthma in children under 12 months of age. Montelukast may be helpful to prevent virus-induced exacerbations in children aged 2–5 years.
[4] Do not use **salmeterol** in children under 4 years of age.

Medication dosing

Table 7. Asthma medications: low and medium dosing

Medication	Low dose	Medium dose
Inhaled short-acting beta$_2$-agonist (SABA)		
Albuterol HFA w/spacer	90 mcg/puff 2 puffs every 4–6 hours prn	—
Inhaled corticosteroids (ICS) [1]		
Additional ICS prescribing notes follow this table.		
Beclomethasone (QVAR) HFA/MDI w/spacer	Age 5–11 years: 40–80 mcg 2x daily Age ≥ 12 years: 40–120 mcg 2x daily	Age 5–11 years: > 80–160 mcg 2x daily Age ≥ 12 years: > 120–240 mcg 2x daily
Budesonide (Pulmicort Respules) nebulization suspension	Age 12 months–4 years: 0.25–0.5 mg, divided 1–2x daily Age 5–11 years: 0.5 mg, divided 1–2x daily	Age 12 months–4 years: > 0.5–1 mg, divided 1–2x daily Age 5–11 years: 1 mg, divided 1–2x daily
Fluticasone (Flovent) HFA/MDI w/facemask and spacer	Age 0–4 years: 176 mcg, divided 2x daily Age 5–11 years: 88–176 mcg, divided 2x daily Age ≥ 12 years: 88–264 mcg, divided 2x daily	Age 0–4 years: > 176–352 mcg, divided 2x daily Age 5–11 years: > 176–352 mcg, divided 2x daily [2] Age ≥ 12 years: > 264–440 mcg, divided 2x daily
Mometasone (Asmanex Twisthaler) [3]	Age 4–11 years: 110 mcg once daily in evening Age ≥ 12 years: 220 mcg once daily in evening	Age 6–11 years: 220 mcg once daily in evening [4] Age ≥ 12 years: 440 mcg, divided 1–2x daily [5]
Long-acting inhaled beta$_2$-agonist (LABA)		
Additional LABA prescribing notes follow this table.		
Salmeterol (Serevent Diskus)	Age ≥ 4 years: 50 mcg every 12 hours	—
Leukotriene modifier (LTRA)		
Montelukast (Singulair)	Age 12 months–5 years: 4 mg daily at bedtime Age 6–14 years: 5 mg daily at bedtime Age ≥ 15 years: 10 mg daily at bedtime	—
Combination ICS/LABA [1]		
Fluticasone/Salmeterol (Advair Diskus)	Age ≥ 4 years: 100 mcg/50 mcg 2x daily, 12 hours apart	Age ≥ 12 years: 250 mcg/50 mcg 2x daily, 12 hours apart

[1] Coverage for Molina patients may be different than that offered by other health plans. Contact Customer Service at 1-888-901-4636 or see the Molina Health Care Formulary (http://www.molinahealthcare.com/members/wa/en-us/mem/medicaid/overvw/coverd/pages/presdrugs.aspx) for a list of preferred medications.

[2] Fluticasone dose is per NHLBI recommendation; however, it exceeds the maximum FDA-approved dose of fluticasone for children aged 4–11 years.

[3] Children need to be observed using the Twisthaler. Children under 6 years of age might not be able to perform proper technique, which would result in the drug being ineffective.

[4] Mometasone dose is per GINA recommendation; however, it exceeds maximum FDA-approved dose of mometasone for children aged 4–11 years.

[5] If taken once daily, dose should be in the evening.

Table 7 prescribing notes: inhaled corticosteroids (ICS)

Impact of ICS use on growth in children

There is evidence that, in children with persistent asthma, regular use of ICS at a low or medium daily dose is associated with an average height reduction of about 0.5 cm in the first year of treatment; however, the growth suppression is less pronounced in the second and third years. In a long-term follow-up study (Kelley 2012) of children with persistent asthma, the mean height was 1.2 centimeters lower in the group who received daily low- or medium-dose ICS therapy than in the placebo group. The majority of benefit from ICS can be achieved at low to medium doses, after which the efficacy curve begins to flatten out. In contrast, the potential for growth inhibition increases at higher doses of ICS.

To minimize its impact on growth, ICS should be prescribed at the lowest effective dose, and growth should be systematically monitored during any ICS treatment of children with persistent asthma. When considering the use of ICS as controller medication, parents need to understand that the exacerbations occurring with uncontrolled asthma might also slow growth, though to lesser extent than the use of ICS, at least in the first year of treatment.

Effectiveness of intermittent ICS use

There is insufficient evidence to determine the effectiveness of intermittent symptom-based (versus continuous) use of ICS in persistent asthma. However, intermittent ICS use may be considered for certain patients who have well-known, predictable asthma triggers that have been confirmed over a series of follow-up visits, regardless of patient age. Patients and families often take it upon themselves to adopt this treatment approach, and open dialogue regarding this approach is encouraged.

Table 7 prescribing notes: FDA black box warnings on use of long-acting beta-agonists (LABAs) in asthma

In 2010 the Food and Drug Administration (FDA) issued a **safety alert** **that LABAs increase the risk of severe exacerbation of asthma symptoms, leading to hospitalizations in pediatric and adult patients as well as death in some patients using LABAs for the treatment of asthma. "**Black box" warnings on this risk were added to all LABA drug labels.

The FDA recommends that:

- **Use of a LABA alone without use of a long-term asthma control medication, such as an ICS, is contraindicated** (absolutely advised against) in the treatment of asthma.
- LABAs should not be used in patients whose asthma is adequately controlled on low- or medium-dose ICS.
- LABAs should only be used as additional therapy for patients with asthma who are currently taking but are not adequately controlled on a long-term asthma control medication, such as an ICS.
- Once asthma control is achieved and maintained, patients should be assessed at regular intervals. Step-down therapy should begin (e.g., discontinue LABA), if possible without loss of asthma control, and the patient should continue to be treated with a long-term asthma control medication, such as an ICS.
- Pediatric and adolescent patients who require the addition of a LABA to an ICS should use a combination product containing both an ICS and a LABA, to ensure adherence with both medications.

In a 2011 drug safety communication, the FDA stated there was insufficient evidence to determine whether concurrent use of an ICS or other long-term controller medication mitigated the risk of asthma-related death with LABA, and requested additional post-marketing safety trials be conducted to assess this. The FDA expects results from these trials in 2017.

Follow-up/Monitoring

After initiating or stepping up medication, it is very important to follow up with patients and assess their response.

When deciding on follow-up intervals, it's helpful to bear in mind that inhaled corticosteroids can take about 4 weeks of regular use to have the most benefit.

Individuals vary widely in their response to and tolerance of specific therapies and drugs, and it is difficult to predict which medications will be both effective and tolerable for an individual patient. The decision of which medication to start with may be based on patient or provider preference or on previous trials with a medication.

Assess asthma control. Talk to patient and assess for the "rule of twos," which holds that if patients have daytime asthma symptoms more than twice a week or nocturnal asthma symptoms more than twice a month, their asthma might not be well-controlled, and a step up in therapy might be indicated. Also assess for activity limitations due to asthma, missed work or school due to asthma, side effects from asthma medications, or any exacerbations since last visit. The Asthma Control Test (ACT) questionnaire is a validated method to assess asthma control and includes most of these questions.

If the first-line preferred medication isn't successful at maximum dose, consider taking these steps before changing the medication:

1. Confirm the asthma diagnosis; a good history and spirometry can be critical here.
2. Address adherence concerns, if indicated.
3. Ask the patient to demonstrate the appropriate metered dose inhaler (MDI) technique. If the patient is having difficulty with the MDI technique, consider adding a spacer or switching to a different device type (e.g., Asmanex Twisthaler, or Pulmicort Flexhaler), which may help to increase adherence. *Note:* Certain groups—such as young children or those with arthritic hands—may have trouble using these alternative devices.

Once steps 1–3 have been completed, consider adding an LTRA or switching to a combination ICS/LABA. If the patient's asthma is still not well controlled on combination therapy, consider referral to Allergy & Asthma.

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 (e.g., symptoms, activity level, measures of lung function) and adjust the dose accordingly. Once asthma control is achieved and sustained for at least 3 months, the dose should be carefully titrated down to the minimum dose necessary to maintain control. However, at times it may be prudent to delay stepping down if exposure to a known trigger is anticipated in the near term (e.g., the September asthma epidemic seen when school starts at the onset of cold and flu season).

To optimize treatment and prevent complications, the following periodic monitoring is advised:

Table 8. Recommended periodic monitoring of conditions and complications

Assessment	Frequency
• Assess asthma control. [1] • Review written Asthma Action Plan. • Assess patient adherence: o Currently taking controller medication? o Taking medication daily? • Determine if therapy should be maintained, stepped down, or stepped up.	Every visit
• Spirometry [2]	At a minimum of every 2 years. Use spirometry more frequently if symptoms are poorly controlled. People whose asthma requires a daily controller to be well controlled may benefit from spirometry every 6 months.

[1] For children aged 4–11 years, use the Childhood Asthma Control Test. Not assessed in children under 4 years old.
[2] Not assessed in children under 5 years old.

Recommended Immunizations for Patients with Asthma

Recommend an annual **flu vaccine** to help patients prevent influenza.

The **pneumococcal polysaccharide vaccine** (PPV23) is now recommended for asthmatic patients aged 19–64 (PPV23 is already recommended for all patients aged 65); see the CDC guideline at http://www.cdc.gov/vaccines/vpd-vac/pneumo/

Referral

Consider a referral to Allergy & Asthma if you have difficulty confirming the diagnosis, or for patients who have:

- Severe asthma that requires treatment beyond Step 4 therapy.
- Persistent uncontrolled asthma or frequent exacerbations after 3–6 months of treatment.
- Required more than two bursts of oral corticosteroids in 1 year or have an exacerbation requiring hospitalization.
- Any risk factors for asthma-related death (history of ICU admission, mechanical ventilation for asthma, confirmed food allergy).
- Other conditions that complicate asthma or its diagnosis (e.g., sinusitis, nasal polyps, aspergillosis, severe rhinitis, vocal cord dysfunction, GERD).
- Evidence of, or risk of, significant treatment side effects.
- Clear relationship between asthma symptoms and exposure to an allergen.

If occupational asthma is suspected, refer to Occupational Medicine.

Evidence Summary

To develop the Asthma Guideline, the guideline team has adapted the following externally developed evidence-based guidelines:

- 2014 Global Initiative For Asthma: Global Strategy for Asthma Management and Prevention
- 2013 Institute for Clinical Systems Improvement (ICSI): Diagnosis and Management of Asthma
- 2013 Kaiser Permanente: Management of Asthma in Children and Adolescents
- 2013 Kaiser Permanente: Children, Adolescents and Adult Asthma Clinical Practice Guideline
- 2012 Agency for Healthcare Research and Quality (AHRQ): Medication Adherence Interventions Comparative Effectiveness. Evidence-based practice
- 2007 National Heart, Lung, and Blood Institute (NHLBI): Guidelines for the Diagnosis and Management of Asthma

Accuracy and reliability of screening and diagnostic tests

Use of spirometry in the diagnosis and initial assessment of asthma

There is fair evidence that objective assessment of pulmonary function using spirometry, in addition to the medical history and physical examination, could improve the diagnosis of asthma and the determination of severity in adults and children 4–18 years of age.

Researchers found that clinical symptoms alone underestimated spirometry-determined severity in 31% of the children, and spirometry alone underestimated clinician-determined severity by 40% (Cowen 2007). An earlier study showed that 49% of the patients predicted to be abnormal with clinical evaluation had normal spirometry, and 10% predicted to be normal clinically had abnormal spirometry (Nair 2005). In another study (Stout 2006), one-third of the children with moderate to severe asthma were reclassified to a more severe category when pulmonary function tests were considered in addition to the symptoms.

Impact of spirometry on management decisions

There is fair evidence that the use of spirometry has an impact on management decisions. There is, however, insufficient evidence to determine that treatment decisions based on spirometry results reduce morbidity and mortality due to asthma.

In Nair and colleagues' 2005 study, providers made the initial treatment decisions before receiving the pulmonary function test results. The treatment decisions were then revised, if needed, after reviewing the results. Based on spirometry results, changes were made in the management decisions for 15% of the patients. In these cases the provider was more likely to increase (75%) than to maintain (20%) or decrease (5%) therapy.

In summary, neither spirometry alone nor history alone is fully adequate. The proper diagnosis and management of asthma requires both spirometry and clinical history.

Assessment of asthma control

Measures for assessing asthma control

There are multiple questionnaires for the assessment of asthma control. These include: the Asthma Control Test (ACT), Asthma Therapy Assessment Questionnaire (ATAQ), Asthma Control Questionnaire (ACQ), Mini Asthma Quality of Life Questionnaire, and others.

There is insufficient evidence to determine the effect of monitoring asthma patients with any of these questionnaires on health outcomes.

There is no established gold standard for assessing asthma control, and there is insufficient evidence to determine that one test is superior to the other in monitoring control. The majority of the questionnaires were validated for assessing asthma control in patients with persistent asthma. However, no published randomized controlled trials (RCTs) compared one questionnaire with the other, nor studied the effect of monitoring asthma patients with any of these questionnaires on health outcomes.

Frequency of periodic monitoring of control

There is insufficient evidence to determine the most appropriate frequency of monitoring for asthma. There were no published trials that compared the effect of different frequencies of visits to the clinician on asthma control and outcomes.

Pharmacologic therapy

Intermittent (symptom-based) versus daily use of inhaled corticosteroids

The published literature does not provide sufficient evidence to determine that intermittent symptom-based use of ICS has superior or equivalent benefits versus daily ICS use in patients with persistent asthma. There is also insufficient evidence to determine the long-term effects of intermittent ICS use on lung growth and lung function decline in patients with persistent asthma.

The overall results of the published RCTs and two recent meta-analyses (Rodrigo 2013, Chauhan 2013) suggest that patients in the daily ICS regimen received significantly higher cumulative doses of ICS versus those in the intermittent symptom-based ICS groups, but with no significant differences in the frequency of asthma exacerbation, number of patients with exacerbations requiring the use of oral corticosteroids, ED visits, hospitalization, serious adverse events, total withdrawals, or withdrawals due to treatment failure. The pediatric trials showed a small decline in the short-term linear growth rate with daily use of ICS (results on statistical significance were conflicting). On the other hand, patients in the intermittent ICS groups had a small improvement in change from baseline peak expiratory flow rate, but had fewer symptom-free days, fewer asthma control days, more use of rescue medication, and an increase from baseline in exhaled nitric oxide.

Effect of inhaled corticosteroids on linear growth of children with persistent asthma

The results of the published meta-analyses and RCTs suggest that the regular use of ICS at low or medium daily dose may be associated with a reduction in linear growth velocity and height (average 0.48 cm/year and 0.61 cm/year, respectively, according to a 2014 meta-analysis by Zhang and colleagues) in children with mild to moderate persistent asthma. The authors performed a subgroup analysis of data from five trials in which treatment was used for > 1 year and found that the significant effect of ICS on growth suppression observed in the first year was less pronounced and not statistically significant between patients receiving ICS versus those in the control groups in the second and third years of treatment (the authors indicate that it is unclear why the difference in growth suppression is less pronounced during subsequent years of treatment versus the first year). A long-term follow-up of a cohort from the CAMP trial (initial age 5–13) (Kelly 2012) suggests that the reduction in height associated with the use of ICS (budesonide) that was observed after 2 years of treatment in pre-pubertal children persisted as a reduction in adult height. This decrease was not progressive or cumulative. In this cohort, the adjusted mean adult height was 1.2 cm lower in the budesonide group than the placebo group (171.1 cm vs. 172.3 cm, respectively, p=0.001). The decrease in growth velocity observed in the budesonide group in the first 2 years of the trial occurred primarily in pre-pubertal participants.

A recent meta-analysis (Pruteanu 2014) that evaluated the ICS dose-response effects on growth in children with persistent asthma showed a small but statistically significant reduction in growth velocity with higher ICS doses.

There is insufficient evidence from head-to-head trials with long-term follow-up to determine the comparative effect of the commonly used ICS formulations, the inhaler used, or the dose on the linear growth of children. Results from RCTs with short-term follow-up suggest that fluticasone propionate has significantly less impact on childhood growth than budesonide or beclomethasone dipropionate given in therapeutically equivalent doses. Pruteanu and colleagues (2014) also noted that fluticasone, ciclesonide, or mometasone may have less suppressive effect on growth compared to budesonide and beclomethasone.

The evidence, however, has to be interpreted with caution as it may be difficult to fully and accurately assess the effect of ICS on growth of children, as growth is affected by several factors that include ethnic and genetic background, sex, age, pubertal status, onset of puberty, nutrition, chronic disease, severity of asthma, and other factors, which may confound the results of studies evaluating the effect

of ICS on growth. In addition, the systemic activity of ICS may be affected by a number of factors, as formulation, pharmacokinetic properties, and delivery system or device may affect the consistency of dosing and effective dose delivered as well as adherence to therapy (Fuhlbrigge 2012). Added to that, the majority of published studies were short-term and did not follow up the patients long enough to assess the effect of ICS on final growth and to determine whether catch-up growth would allow them to reach their growth potential.

Step-up therapy for children with uncontrolled asthma while receiving ICS

The Best Add-on Therapy Giving Effective Responses (BADGER) trial (Lemanske 2010) evaluated the differential response to three step-up therapies for children 6–17 years of age with uncontrolled mild to moderate asthma while on low-dose inhaled corticosteroids. The study also aimed at identifying patient characteristics that could be used to predict the response to step-up treatment.

The primary outcomes of the trial were differential response to the step-up therapies based on need for oral prednisone for acute exacerbations, number of asthma control days, and FEV_1.

The results of the study show that a higher proportion had a better response to LABA than to LTRA (52% vs. 34%, p=0.02) and a better response to LABA than to high-dose ICS (54% vs. 32%, p=0.004), without significant differences between LTRA and high-dose ICS.

There is insufficient published evidence to determine the relative long-term safety of the three regimens.

Comparative effectiveness and safety of montelukast (Singulair) versus inhaled corticosteroids (ICS) in patients with mild to moderate asthma

There is evidence form a valid meta-analysis (Castro-Rodriguez 2010) of 18 RCTs (N=3,757) that compared to montelukast, ICS leads to better asthma control and lung function, and fewer asthma exacerbations requiring systemic steroids among school-age children and adolescents with mild to moderate persistent asthma.

The meta-analysis does not provide sufficient evidence to determine whether the addition of montelukast to ICS would improve outcomes.

Long-acting beta$_2$ agonists (LABAs)

There is evidence that LABAs used alone may increase the risk of asthma-related fatal and nonfatal adverse events.

Combination corticosteroid/beta-agonist in a single inhaler as a maintenance and reliever therapy

The results of published studies and meta-analyses (including Patel 2013, Papi 2013, Cates 2013, and Kew 2013) suggest that exacerbation rates of asthma are reduced with the use of single inhaler therapy budesonide/formoterol as maintenance and reliever therapy (SMART regimen) versus conventional treatment (ICS alone at equivalent or higher doses, or fixed-dose ICS/LABA combination) with additional SABA as needed for rescue, in patients whose asthma is not controlled with low-dose ICS.

The evidence is mixed regarding the effect of single inhaler therapy budesonide/formoterol as maintenance and reliever therapy on reducing hospitalization. The Cates and Karner systematic review (2013) did not show a significant benefit of the therapy in reducing hospitalization, while Kew and colleagues' 2013 meta-analysis showed a significant reduction in hospitalization or ED visits due to exacerbations among the groups using the SMART regimen.

The published literature does not provide sufficient evidence to determine the optimal number of puffs, threshold, or timing for increasing the budesonide/formoterol (or alternative combination) dose to protect against severe exacerbations.

There is also insufficient evidence to determine the long-term benefits and safety of the single inhaler therapy budesonide/formoterol as maintenance and reliever therapy. All published trials on the SMART regimen (with the exception of one trial conducted in New Zealand) were funded by AstraZeneca, the pharmaceutical company that markets Symbicort. Many of the studies had the

treatment of symptomatic patients stepped down during the run-in phase, which would have had an impact on the results as patients in the control group may have been undertreated. The patients in the trials received specific training on the technique for using inhalers and were regularly followed up, which may limit generalization of the results to patients in a non-controlled real-life setting.

References

Cates CJ, Karner C. Combination formoterol and budesonide as maintenance and reliever therapy versus current best practice (including inhaled steroid maintenance), for chronic asthma in adults and children. *Cochrane Database Syst Rev*. 2013 Apr 30; 4:CD007313. doi: 10.1002/14651858. CD007313.pub3.

Chauhan BF, Chartrand C, Ducharme FM. Intermittent versus daily inhaled corticosteroids for persistent asthma in children and adults. *Cochrane Database Syst Rev.* 2013 Feb 28; 2:CD009611. doi: 10.1002/14651858.CD009611.pub3.

Cowen MK, Wakefield DB, Cloutier MM. Classifying asthma severity: objective versus subjective measures. *J Asthma.* 2007 Nov;44(9):711-715.

Fuhlbrigge AL, Kelly H. Inhaled corticosteroids in children: effects on bone mineral density and growth. *Lancet Respir Med.* 2014 Jun; 2(6):487-496.doi: 10.1016/S2213-2600(14)70024-4.

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 Sep 6;367(10):904-912.

Kew KM, Karner C, Mindus SM, Ferrara G. Combination formoterol and budesonide as maintenance and reliever therapy versus combination inhaler maintenance for chronic asthma in adults and children. *Cochrane Database Syst Rev.* 2013 Dec 16; 12:CD009019. doi: 10.1002/14651858.CD009019.pub2.

Lemanske RF Jr, Mauger DT, Sorkness CA, et al; Childhood Asthma Research and Education (CARE) Network of the National Heart, Lung, and Blood Institute. Step-up therapy for children with uncontrolled asthma receiving inhaled corticosteroids. *N Engl J Med.* 2010 Mar 18;362(11):975-985.

Nair SJ, Daigle KL, DeCuir P, Lapin CD, Schramm CM. The influence of pulmonary function testing on the management of asthma in children. *J Pediatr.* 2005 Dec;147(6):797-801.

Papi A, Corradi M, Pigeon-Francisco C, et al. Beclometasone-formoterol as maintenance and reliever treatment in patients with asthma: a double-blind, randomised controlled trial*. Lancet Respir Med*. 2013 Mar; 1(1):23-31.

Patel M, Pilcher J, Pritchard A, et al; SMART Study Group. Efficacy and safety of maintenance and reliever combination budesonide-formoterol inhaler in patients with asthma at risk of severe exacerbations: a randomised controlled trial*. Lancet Respir Med*. 2013 Mar;1(1):32-42.

Pruteanu AI, Chauhan BF, Zhang L, Prietsch SO, Ducharme FM. Inhaled corticosteroids in children with persistent asthma: dose-response effects on growth. *Cochrane Database Syst Rev*. 2014 Jul 17; 7:CD009878. doi: 10.1002/14651858.CD009878.pub2.

Rodrigo GJ, Castro-Rodríguez JA. Daily vs. intermittent inhaled corticosteroids for recurrent wheezing and mild persistent asthma: a systematic review with meta-analysis. *Respir Med*. 2013 Aug;107(8):1133-1140.

Stout JW, Visness CM, Enright P, et al. Classification of asthma severity in children: the contribution of pulmonary function testing. *Arch Pediatr Adolesc Med*. 2006 Aug;160(8):844-850.

Zhang L, Prietsch SO, Ducharme FM. Inhaled corticosteroids in children with persistent asthma: effects on growth. *Cochrane Database Syst Rev*. 2014 Jul 17;7:CD009471. doi: 10.1002/14651858. CD009471.pub2.

Guideline Development Process and Team

The Asthma Guideline was developed using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis. For details, see Evidence Summary and References.

This edition of the guideline was approved for publication by the Guideline Oversight Group in July 2015.

Team

The Asthma Guideline development team included representatives from the following specialties: allergy, family medicine, nursing operations, pediatrics, pharmacy, pulmonary medicine, and residency.

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Disclosure of conflict of interest

Kaiser Permanente requires that team members participating on a guideline team disclose and resolve all potential conflicts of interest that arise from financial relationships between a guideline team member or guideline team member's spouse or partner and any commercial interests or proprietary entity that provides or produces health care-related products and/or services relevant to the content of the guideline.

Team members listed below have disclosed that their participation on the Asthma Guideline team includes no promotion of any commercial products or services, and that they have no relationships with commercial entities to report.

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Grant/research support: Patient-Centered Outcomes Research Institute

Childhood Asthma Control Test for children 4 to 11 years.

This test will provide a score that may help the doctor determine if your child's asthma treatment plan is working or if it might be time for a change.

How to take the Childhood Asthma Control Test

Step 1 Let your child respond to the first four questions (1 to 4). If your child needs help reading or understanding the question, you may help, but let your child select the response. Complete the remaining three questions (5 to 7) on your own and without letting your child's response influence your answers. There are no right or wrong answers.

Step 2 Write the number of each answer in the score box provided.

Step 3 Add up each score box for the total.

Step 4 Take the test to the doctor to talk about your child's total score.

19 or less

If your child's score is 19 or less, it may be a sign that your child's asthma is not controlled as well as it could be. Bring this test to the doctor to talk about the results.

Have your child complete these questions.

1. How is your asthma today?

SCORE				
	0  Very bad	1  Bad	2  Good	3  Very good

2. How much of a problem is your asthma when you run, exercise or play sports?

	0  It's a big problem, I can't do what I want to do.	1  It's a problem and I don't like it.	2  It's a little problem but it's okay.	3  It's not a problem.

3. Do you cough because of your asthma?

	0  Yes, all of the time.	1  Yes, most of the time.	2  Yes, some of the time.	3  No, none of the time.

4. Do you wake up during the night because of your asthma?

	0  Yes, all of the time.	1  Yes, most of the time.	2  Yes, some of the time.	3  No, none of the time.

Please complete the following questions on your own.

5. During the last 4 weeks, how many days did your child have any daytime asthma symptoms?

5 Not at all	4 1-3 days	3 4-10 days	2 11-18 days	1 19-24 days	0 Everyday

6. During the last 4 weeks, how many days did your child wheeze during the day because of asthma?

5 Not at all	4 1-3 days	3 4-10 days	2 11-18 days	1 19-24 days	0 Everyday

7. During the last 4 weeks, how many days did your child wake up during the night because of asthma?

5 Not at all	4 1-3 days	3 4-10 days	2 11-18 days	1 19-24 days	0 Everyday

TOTAL

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FOR PATIENTS:

Take the Asthma Control Test™ (ACT) for people 12 years and older.

Know your score. Share your results with your doctor.

Step 1 Write the number of each answer in the score box provided.
Step 2 Add the score boxes for your total.
Step 3 Take the test to the doctor to talk about your score.

1. In the past **4 weeks**, how much of the time did your asthma keep you from getting as much done at work, school or at home?

All of the time (1)	Most of the time (2)	Some of the time (3)	A little of the time (4)	None of the time (5)

2. During the past **4 weeks**, how often have you had shortness of breath?

More than once a day (1)	Once a day (2)	3 to 6 times a week (3)	Once or twice a week (4)	Not at all (5)

3. During the past **4 weeks**, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?

4 or more nights a week (1)	2 or 3 nights a week (2)	Once a week (3)	Once or twice (4)	Not at all (5)

4. During the past **4 weeks**, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?

3 or more times per day (1)	1 or 2 times per day (2)	2 or 3 times per week (3)	Once a week or less (4)	Not at all (5)

5. How would you rate your asthma control during the past **4 weeks**?

Not controlled at all (1)	Poorly controlled (2)	Somewhat controlled (3)	Well controlled (4)	Completely controlled (5)

SCORE ☐

TOTAL ☐

If your score is 19 or less, your asthma may not be controlled as well as it could be. Talk to your doctor.

FOR PHYSICIANS:

The ACT is:
- A simple, 5-question tool that is self-administered by the patient
- Clinically validated by specialist assessment and spirometry[1]
- Recognized by the National Institutes of Health

Reference: 1. Nathan RA et al. J Allergy Clin Immunol. 2004;113:59-65.

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