Asthma Diagnosis and Treatment Guideline

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Last guideline approval: February 2021

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.
Major Changes as of February 2021

- Intermittent use of inhaled corticosteroids (ICS) may be considered for patients with mild intermittent asthma symptoms. However, continuing daily ICS is recommended for patients with persistent asthma.
- A new section on managing asthma exacerbations was added.
- A new section on managing exercise-induced bronchospasm was added.
- The asthma SmartSet for Primary Care has been updated with new and updated SmartPhrases for initial evaluation, follow-up, asthma history, asthma control, exacerbations, spirometry, and inhalation treatment for both children and adults.

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.

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:

A. **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

B. **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 FEV₁ from baseline. In adults, an increase in FEV₁ 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
   - See the Spirometry Practice Resources in Clinical Library for more information: [https://cl.kp.org/wa/cpg/practice-resources/spirometry-practice-resources.html](https://cl.kp.org/wa/cpg/practice-resources/spirometry-practice-resources.html)

C. **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). The SmartPhrase .asthmaseverity walks the provider through classifying and documenting the severity of the patient’s asthma.

**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.

<table>
<thead>
<tr>
<th>Impairment (Over last 2–4 weeks)</th>
<th>Intermittent asthma</th>
<th>Persistent asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td>≤ 2 days/week</td>
<td>≥ 3 days/week but not daily</td>
</tr>
<tr>
<td><strong>Nighttime awakenings</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age ≥ 5 years</td>
<td>≤ 2 nights/month</td>
<td>3–4 nights/month &gt; 1 night/week but not nightly</td>
</tr>
<tr>
<td>Age &lt; 5 years</td>
<td>None</td>
<td>1–2 nights/month 3–4 nights/month</td>
</tr>
<tr>
<td><strong>Short-acting beta2-agonist use (for rescue, not exercise prophylaxis)</strong></td>
<td>≤ 2 days/week ¹</td>
<td>≥ 3 days/week but ≤ 1x/day Daily</td>
</tr>
<tr>
<td><strong>Interference with normal activity</strong></td>
<td>None</td>
<td>Minor limitation</td>
</tr>
<tr>
<td><strong>Lung function</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV₁ predicted or personal best</td>
<td>Normal ² between exacerbations; 80%</td>
<td>&gt; 80% 60–80% &lt; 60%</td>
</tr>
<tr>
<td>FEV₁ /FVC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age ≥ 12 years</td>
<td>Normal ²</td>
<td>Normal ² Reduced 5% Reduced &gt; 5%</td>
</tr>
<tr>
<td>Age 5–11 years</td>
<td>&gt; 85%</td>
<td>&gt; 80% 75–80% &lt; 75%</td>
</tr>
</tbody>
</table>

¹ ≤ 2 days/week of short-acting beta2-agonist for rescue means ≤ 2 doses (4 puffs) per week.

² Normal FEV₁ /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, and is classified as:

- Well controlled,
- Not well controlled, or
- 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.

The SmartPhrases for asthma control are broken down by age—.asthmacontrol<5, .asthmacontrol5to11yo, and .asthmacontrol>12—and allow the provider to document degree of impairment and asthma control in the note.

Patients aged < 5 years

| Table 2. Patients aged < 5 years currently taking medications: asthma control assessment and treatment recommendations
<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical assessment</th>
<th>Asthma is:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Well controlled</strong></td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td>≤ 2 days/week</td>
</tr>
<tr>
<td><strong>Nighttime awakenings</strong></td>
<td>≤ 1x/month</td>
</tr>
<tr>
<td><strong>Short-acting beta₂ agonist use (for rescue, not exercise prophylaxis)</strong></td>
<td>≤ 2 days/week ¹</td>
</tr>
<tr>
<td><strong>Interference with normal activity</strong></td>
<td>None</td>
</tr>
<tr>
<td><strong>Exacerbations requiring systemic corticosteroids</strong></td>
<td>≤ 1x/year</td>
</tr>
</tbody>
</table>

**Treatment recommendation**

*Note:* Before stepping up therapy, review the patient’s adherence to medication, inhaler technique, and environmental control, and consider alternative diagnoses.

<table>
<thead>
<tr>
<th>Treatment recommendation</th>
<th><strong>Well controlled</strong></th>
<th><strong>Not well controlled</strong></th>
<th><strong>Very poorly controlled</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintain therapy at current step. If well controlled for 3 months or longer, consider step down.</td>
<td></td>
<td>Step up 1 step.</td>
<td>Step up 1–2 steps. Consider short course of systemic corticosteroids.</td>
</tr>
</tbody>
</table>

**Follow-up**

See “Follow-up/Monitoring” (p. 12) for more information.

<table>
<thead>
<tr>
<th>Follow-up</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1–6 months</td>
<td>2–6 weeks</td>
</tr>
</tbody>
</table>

¹ ≤ 2 days/week of short-acting beta₂-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.

<table>
<thead>
<tr>
<th>Clinical assessment</th>
<th>Asthma is:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Well controlled</td>
</tr>
<tr>
<td>Symptoms</td>
<td>≤ 2 days/week</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>≤ 1x/month</td>
</tr>
<tr>
<td>Short-acting beta-agonist use (for rescue, not exercise prophylaxis)</td>
<td>≤ 2 days/week</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
</tr>
<tr>
<td>Exacerbations requiring systemic corticosteroids</td>
<td>≤ 1x/year</td>
</tr>
</tbody>
</table>

**Childhood Asthma Control Test (ACT) questionnaire**

Consider use as an adjunct objective measure to the clinical assessment. Must be confirmed by follow-up discussion.

<table>
<thead>
<tr>
<th>ACT score</th>
<th>Well controlled</th>
<th>Not well controlled</th>
<th>Very poorly controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 20</td>
<td></td>
<td>13–19</td>
<td>≤ 12</td>
</tr>
</tbody>
</table>

The ACT questionnaire is available as a flow sheet in KP HealthConnect and a paper version through Print Shop.

**Lung function (spirometry)**

Consider use as an adjunct objective measure to the clinical assessment in patients who have poor response to treatment.

<table>
<thead>
<tr>
<th>FEV₁, predicted</th>
<th>Well controlled</th>
<th>Not well controlled</th>
<th>Very poorly controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 80%</td>
<td></td>
<td>60–80%</td>
<td>&lt; 60%</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>&gt; 0.80</td>
<td>0.75–0.80</td>
<td>&lt; 0.75</td>
</tr>
</tbody>
</table>

### Treatment recommendations

- **Note:** Before stepping up therapy, review the patient’s adherence to medication, inhaler technique, and environmental control, and consider alternative diagnoses.
- **Well controlled:** Maintain therapy at current step. If well controlled for 3 months or longer, consider step down.
- **Not well controlled:** Step up at least 1 step.
- **Very poorly controlled:** Step up 1–2 steps. Consider short course of systemic corticosteroids.

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>1–6 months</th>
<th>2–6 weeks</th>
<th>2 weeks</th>
</tr>
</thead>
</table>

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

<table>
<thead>
<tr>
<th>Clinical assessment</th>
<th>Asthma is:</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Well controlled</td>
<td>Not well controlled</td>
<td>Very poorly controlled</td>
</tr>
<tr>
<td>Symptoms</td>
<td>≤ 2 days/week</td>
<td>&gt; 2 days/week</td>
<td>Throughout the day</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>≤ 2x/month</td>
<td>1–3x/week</td>
<td>≥ 4x/week</td>
</tr>
<tr>
<td>Short-acting beta₂-agonist use (for rescue, not exercise prophylaxis)</td>
<td>≤ 2 days/week</td>
<td>&gt; 2 days/week</td>
<td>Several times a day</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
<td>Some limitation</td>
<td>Extreme limitation</td>
</tr>
<tr>
<td>Exacerbations requiring systemic corticosteroids</td>
<td>≤ 1x/year</td>
<td>≥ 2x/year</td>
<td>≥ 2x/year</td>
</tr>
</tbody>
</table>

**Adult Asthma Control Test (ACT) questionnaire**
Consider use as an adjunct objective measure to the clinical history. Must be confirmed by follow-up discussion.

<table>
<thead>
<tr>
<th>ACT score</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 20</td>
<td>16–19</td>
</tr>
<tr>
<td>≤ 15</td>
<td></td>
</tr>
</tbody>
</table>

The ACT questionnaire is available as a flow sheet in KP HealthConnect and a paper version through Print Shop.

*Note:* ACT question 4 is asking about how often short-acting beta₂-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.

<table>
<thead>
<tr>
<th>FEV₁ predicted or personal best</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 80%</td>
<td>60–80%</td>
</tr>
<tr>
<td>&lt; 60%</td>
<td></td>
</tr>
</tbody>
</table>

**Treatment recommendation**
*Note:* Before stepping up therapy, review the patient’s adherence to medication, inhaler technique, and environmental control, and consider alternative diagnoses.

<table>
<thead>
<tr>
<th>Well controlled</th>
<th>Not well controlled</th>
<th>Very poorly controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintain therapy at current step. If well controlled for 3 months or longer, consider step down.</td>
<td>Step up at least 1 step.</td>
<td>Step up 1–2 steps. Consider short course of systemic corticosteroids.</td>
</tr>
</tbody>
</table>

**Follow-up**
See “Follow-up/Monitoring” (p. 12) for more information.

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1–6 months</td>
<td>2–6 weeks</td>
<td>2 weeks</td>
</tr>
</tbody>
</table>

*1* ≤ 2 days/week of short-acting beta₂-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**
   
   An extensive collection of asthma resources is available on KP.org.
   - 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 KP.org.
   - **Follow an Asthma Action Plan.** 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. There are two versions available: .avsasthmaactionplan is based on symptoms alone (see pamphlet) and .avsasthmaactionplanpeakflows is based on both symptoms and peak flow (see pamphlet). Consider handing out the ACT questionnaire to parents and patients to identify when their asthma might not be well controlled.
   - **Take medication correctly.** Links to patient instructions for using inhalers and devices are available on KPWA Clinical Library.
   - **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 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 and Nicotine Cessation Guideline for recommendations.
   - **Encourage weight management.** See the Weight Management Guideline for recommendations.

4. ** Treat comorbid conditions that worsen asthma**
   These include: allergic bronchopulmonary aspergillosis, environmental allergies, GERD, obesity, obstructive sleep apnea, rhinitis, sinusitis, stress or depression, and 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 of 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 encourages the use of controller medications for persistent asthma. The Asthma Medication Management measure encourages patient adherence to controller medications.

### Asthma Medication Ratio (AMR) HEDIS measure
The percentage of members 5–65 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.

### Asthma Medication Management HEDIS measure
The percentage of members 5–65 years of age who were identified as having persistent asthma and were dispensed appropriate medications which they remained on for 50% and 75% of the treatment period.

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 KP HealthConnect, 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>
<thead>
<tr>
<th>Population</th>
<th>Intermittent asthma</th>
<th>Persistent asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild</td>
<td>Moderate</td>
</tr>
<tr>
<td>Age &lt; 5 years</td>
<td>Step 1</td>
<td>Step 2</td>
</tr>
<tr>
<td>Age 5–11 years</td>
<td>Step 1</td>
<td>Step 2</td>
</tr>
<tr>
<td>Age ≥ 12 years</td>
<td>Step 1</td>
<td>Step 2</td>
</tr>
</tbody>
</table>

\(^1\) Consider short course of systemic corticosteroids.
\(^2\) Using medium-dose inhaled corticosteroid option.
Stepwise approach to long-term asthma control

Prescribing notes follow Table 6.

### Table 6. Stepwise approach to long-term asthma control

Asterisks (*) indicate drugs with FDA Boxed Warnings; see Prescribing Note D.

<table>
<thead>
<tr>
<th>Step</th>
<th>Age &lt; 5 years</th>
<th>Age 5–11 years</th>
<th>Age ≥ 12 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>The medications below may not be appropriate for all patients in this age range. See Prescribing Note A.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td><strong>All ages:</strong> SABA – albuterol. Quick-relief medication as needed.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td><strong>All ages:</strong> Consider intermittent ICS dosing. See Prescribing Note B.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
|      | **ICS low dose**  
1st line: Fluticasone  
2nd line: Budesonide | **Preferred ICS low dose**  
1st line: Fluticasone  
or  
1st line: Ciclesonide (Alvesco) | **Preferred ICS low dose**  
1st line: Ciclesonide (Alvesco)  
2nd line: Mometasone |
|      | **Alternative**  
LTRA – montelukast * | **Alternative**  
LTRA – montelukast * | **Alternative**  
LTRA – montelukast * |
| 3    | **ICS medium dose**  
1st line: Fluticasone  
2nd line: Budesonide | **Preferred ICS medium dose**  
1st line: Fluticasone  
or  
1st line: Ciclesonide (Alvesco) | **Preferred ICS medium dose**  
1st line: Ciclesonide (Alvesco)  
2nd line: Mometasone |
|      | **Alternative**  
ICS/LABA low dose – fluticasone/salmeterol  
or  
LTRA – montelukast * | **Alternative**  
ICS/LABA low dose – fluticasone/salmeterol  
or  
LTRA – montelukast * | **Alternative**  
ICS low dose  
1st line: Ciclesonide (Alvesco)  
2nd line: Mometasone  
plus  
LTRA – montelukast * |
| 4    | **ICS medium dose**  
1st line: Fluticasone  
2nd line: Budesonide  
**plus either**  
LTRA – montelukast *  
or  
LABA – salmeterol * | **Preferred ICS/LABA medium dose** – fluticasone/salmeterol | **Preferred ICS/LABA medium dose** – fluticasone/salmeterol |
|      | **Alternative**  
ICS medium dose  
1st line: Fluticasone  
2nd line: Ciclesonide (Alvesco)  
plus  
LTRA – montelukast *  
or  
Daily and PRN combination medium dose budesonide/ formoterol (Symbicort). See Prescribing Note E. | **Alternative**  
ICS medium dose  
1st line: Ciclesonide (Alvesco)  
2nd line: Mometasone  
plus  
LTRA – montelukast *  
or  
Daily and PRN combination medium dose budesonide/ formoterol (Symbicort). See Prescribing Note E. | **Alternative**  
ICS medium dose  
1st line: Ciclesonide (Alvesco)  
2nd line: Mometasone  
plus  
LTRA – montelukast *  
or  
Daily and PRN combination medium dose budesonide/ formoterol (Symbicort). See Prescribing Note E. |

**Table 6 prescribing notes: stepwise approach to asthma control**

**A. Medication age ranges for patients < 5 YEARS**
Fluticasone
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.

Budesonide
Do not use budesonide in children under 12 months of age. For children aged 1 through 5 years, use budesonide inhalation suspension. Pulmicort Flexhaler is approved only for ages > 5 years.

Montelukast (Singulair)
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.
See Note D re: FDA Boxed Warning.

LABA alone (Salmeterol)
Do not use salmeterol in children under 4 years of age.
See Note D re: FDA Boxed Warning

B. Intermittent use of inhaled corticosteroids (ICS)
For patients with mild intermittent asthma symptoms, intermittent use of ICS can be considered. Some patients may opt for daily ICS on a seasonal basis (e.g., in fall and winter) when they are more likely to have a flare-up associated with a viral illness, and intermittent use during other parts of the year. If ICS is used for a flare-up, it is recommended that it be continued for 2–4 weeks after symptoms have subsided.

C. Impact of ICS 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/0.2 inches in the first year of treatment; however, the growth suppression is less pronounced in the second and third years.

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. Since the impact on growth for ICS use is small (0.5 cm/0.2 inches), withholding steroid use to avoid growth inhibition is not recommended.

D. FDA Boxed Warnings
Montelukast (Singulair)
The FDA is requiring a Boxed Warning stating that serious mental health side effects that may include suicidal thoughts or actions have been reported in patients taking the asthma and allergy medicine montelukast (Singulair). Reserve use for patients with allergic rhinitis who have an inadequate response or intolerance to alternative therapies. In patients with asthma or exercise-induced bronchoconstriction, consider the benefits and risks before use.
https://www.fda.gov/media/135840/download

LABA alone (Salmeterol) in asthma
Using LABAs alone to treat asthma without an ICS to treat lung inflammation is associated with an increased risk of asthma-related death. Therefore, a Boxed Warning is printed on the labels of all single-ingredient LABA medicines approved to treat asthma, COPD, and wheezing caused by exercise. The labels of medicines that contain both an ICS and LABA also retain a Warning and Precaution related to the increased risk of asthma-related death when LABAs are used without an ICS to treat asthma.

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.
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.

E. SMART (Symbicort)

SMART (single-inhaler for maintenance and reliever therapy) is using a single inhaler for both daily maintenance and quick relief. SMART simplifies asthma treatment by avoiding confusion about which inhaler to use and by relying on a single inhalational technique. Because of the quick onset of action of formoterol, the ICS/LABA budesonide/formoterol (Symbicort) can be used as SMART. Symbicort is a non-preferred inhaler and requires Prior Authorization for patients with commercial prescription insurance. It may be cost-prohibitive for some patients. Patients interested in SMART should be referred to Allergy and advised to check with Member Services about coverage.
Medication dosing

Links to [patient instructions for using inhalers and devices](#) are available on KPWA Clinical Library.

### Table 7. Asthma medications: low and medium dosing

<table>
<thead>
<tr>
<th>Medication</th>
<th>Low dose</th>
<th>Medium dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inhaled short-acting beta₂-agonist (SABA)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuterol HFA w/spacer</td>
<td>90 mcg/puff, 2 puffs every 4–6 hours prn</td>
<td>—</td>
</tr>
<tr>
<td><strong>Inhaled corticosteroids (ICS)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciclesonide (Alvesco) HFA/MDI w/spacer</td>
<td>Age 5–11 years: 80 mcg daily</td>
<td>Age 5–11 years: &gt; 80–160 mcg daily</td>
</tr>
<tr>
<td></td>
<td>Age ≥ 12 years: 80–160 mcg daily</td>
<td>Age ≥ 12 years: &gt; 160–320 mcg daily</td>
</tr>
<tr>
<td>Budesonide (Pulmicort Respules) nebulization suspension</td>
<td>Age 12 months–4 years: 0.25–0.5 mg, divided 1–2x daily</td>
<td>Age 12 months–4 years: &gt; 0.5–1 mg, divided 1–2x daily</td>
</tr>
<tr>
<td></td>
<td>Age 5–11 years: 0.5 mg, divided 1–2x daily</td>
<td>Age 5–11 years: 1 mg, divided 1–2x daily</td>
</tr>
<tr>
<td><strong>Fluticasone (Flovent)</strong> HFA/MDI w/facemask and spacer</td>
<td>Age 0–4 years: 176 mcg, divided 2x daily</td>
<td>Age 0–4 years: &gt; 176–352 mcg, divided 2x daily</td>
</tr>
<tr>
<td></td>
<td>Age 5–11 years: 88–176 mcg, divided 2x daily</td>
<td>Age 5–11 years: &gt; 176–352 mcg, divided 2x daily</td>
</tr>
<tr>
<td></td>
<td>Age ≥ 12 years: 88–264 mcg, divided 2x daily</td>
<td>Age ≥ 12 years: &gt; 264–440 mcg, divided 2x daily</td>
</tr>
<tr>
<td><strong>Mometasone (Asmanex HFA)</strong> HFA/MDI w/spacer</td>
<td>Age 5–11 years: 100 mcg once daily in evening</td>
<td>Age 5–11 years: 100 mcg twice daily</td>
</tr>
<tr>
<td></td>
<td>Age ≥ 12 years: 100 mcg twice daily</td>
<td>Age ≥ 12 years: 200 mcg twice daily</td>
</tr>
<tr>
<td><strong>Leukotriene modifier (LTRA)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Montelukast (Singulair)</td>
<td>Age 12 months–5 years: 4 mg daily at bedtime</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Age 6–14 years: 5 mg daily at bedtime</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Age ≥ 15 years: 10 mg daily at bedtime</td>
<td></td>
</tr>
<tr>
<td><strong>Combination ICS/LABA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluticasone/Salmeterol DPI (Wixela Inhub)</td>
<td>Age ≥ 4 years: 100/50 mcg, 1 puff 2x daily</td>
<td>Age ≥ 12 years: 250/50 mcg, 1 puff 2x daily</td>
</tr>
<tr>
<td>Fluticasone/Salmeterol HFA/MDI (Advair HFA)</td>
<td>Age ≥ 4 years: 45/21 mcg, 2 puffs 2x daily</td>
<td>Age ≥ 12 years: 115/21 mcg, 2 puffs 2x daily</td>
</tr>
<tr>
<td>Budesonide/formoterol (Symbicort)</td>
<td>Age ≥ 4 years: 80 mcg/4.5 mcg, 2 puffs 2x daily</td>
<td>Age ≥ 12 years: 160 mcg/4.5 mcg, 2 puffs 2x daily</td>
</tr>
</tbody>
</table>

1 Coverage for Molina patients may be different than that offered by other health plans. Contact Member Services or see the Molina Health Care Formulary 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.
Management of Exercise-Induced Bronchospasm (EIB)

Primary symptoms of EIB include wheezing, chest tightness, shortness of breath (dyspnea), and cough; symptoms can also include chest pain (primarily in children), excessive mucus production, or a feeling of being out of shape when the patient is actually in good physical condition. EIB is common in patients with asthma but may also occur in patients without chronic asthma.

Spirometry is helpful for diagnosis; spirometry results are typically normal in patients with EIB. If spirometry shows airway obstruction with reversibility suggestive of persistent asthma, the underlying asthma should be treated; this will often reduce the EIB. If baseline spirometry is normal, the clinical history is consistent with EIB, and the patient has a good response to preventative therapy, no additional investigation is recommended.

Treatment recommendations include as-needed and pre-exercise use of SABA. To reduce tolerance, daily use of SABA is not recommended. Patients who do not respond to SABA should be referred to Allergy.

While leukotriene receptor antagonists (LTRAs), such as montelukast, can be considered for EIB, there is concern that they may be associated with a risk of behavior- and mood-related changes, including suicidal thoughts, in both adults and children (FDA black box warning, updated May 2020). There is insufficient evidence to determine if this is a causal association. Because of the potential risk of mental health side effects, the benefits of montelukast may not outweigh the risks in some patients, particularly when the symptoms of disease are mild and adequately treated with other medicines.

Management of Asthma Exacerbations

An asthma exacerbation is defined as progressively worsening shortness of breath, cough, wheezing, and chest tightness—or some combination of these symptoms—resulting from decreased expiratory airflow.

Do not routinely perform chest X-ray or arterial blood gases to evaluate exacerbations. Do not routinely prescribe antibiotics to treat asthma exacerbations.

Management of asthma exacerbations in Primary Care

Assess the severity of exacerbation and complete a history and physical exam, including peak flow, measure O2 sat.

- For mild to moderate cases, administer SABA repeatedly (up to 4 puffs every 20 minutes) for the first hour. No additional SABA is needed if there is good initial response. Severe cases should be routed to Urgent Care.
- If symptoms improve and O2 saturation > 94% on room air, continue SABA as needed, start or step up controller, and prescribe prednisone for 5–7 days (3–5 days for children).
- Follow-up in 2–7 days (1–2 days for children).

Management of asthma exacerbations in Acute Care

- Measure peak flow.
- Give O2 by nasal canula or mask to achieve arterial saturation of 93-95% (94-98% in children aged 6-11 years.)
- Administer SABA frequently, preferably via metered dose inhaler (MDI) and spacer (up to 4 puffs every 20 minutes). After the first hour administer 4–10 puffs every 3–4 hours, up to 6–10 puffs every 1–2 hours or more often.
- Give systemic corticosteroids, except for mild exacerbations, in the first hour of presentation. Oral is as effective as IV; continue oral steroids for 5–7 days.
- Consider ipratropium bromide if not responding adequately to SABA.
- Consider IV magnesium sulphate for severe cases with inadequate response to intensive initial treatment.
- Decide on need for hospitalization based on clinical status, symptoms, lung function response to treatment, history of exacerbations, and ability to manage at home.
Follow-up/Monitoring

After initiating or stepping up medication, it is very important to follow up in about 4–6 weeks 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.

Consider using the Asthma Primary Care SmartSet or the available SmartPhrases for your follow-up and monitoring: .asthmacontrol can help you decide if a patient’s asthma is well controlled, and .asthmahistory is useful for reviewing the diagnosis and history of a patient’s asthma care.

If you prefer a full note template, .asthnamini is an asthma follow-up progress note.

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., 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.

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

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Frequency</th>
</tr>
</thead>
</table>
| • 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.

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**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/](http://www.cdc.gov/vaccines/vpd-vac/pneumo/)

**Referral**

Consider a referral to Allergy if you are considering SMART therapy or having 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

The Asthma Guideline was developed using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis.

As part of our improvement process, the Kaiser Permanente Washington guideline team is working towards developing new clinical guidelines and updating the current guidelines regularly. To achieve this goal, we are adapting evidence-based recommendations from high-quality national and international external guidelines, if available and appropriate. The external guidelines should meet several quality standards to be considered for adaptation. They must: be developed by a multidisciplinary team with no or minimal conflicts of interest; be evidence-based; address a population that is reasonably similar to our population; and be transparent about the frequency of updates and the date the current version was completed.

In addition to identifying the recently published guidelines that meet the above standards, a literature search was conducted to identify studies relevant to the key questions that are not addressed by the external guidelines.

External guidelines eligible for adapting


Key questions

1. In children aged ≥ 5 years, adolescents, and adults with persistent asthma, what is the comparative safety and effectiveness of intermittent use of inhaled corticosteroids (ICS) with as-needed SABA versus regular daily use of ICS with as-needed SABA in controlling symptoms and reducing the risk of asthma exacerbations?

The literature search for recent meta-analyses and randomized controlled trials (RCTs) on the comparative effectiveness of intermittent versus daily use of inhaled corticosteroids in the management of persistent asthma identified a review conducted for the Agency for Healthcare Research and Quality (AHRQ) (Sobieraj 2018) and a small short-term trial (Camargos 2018).

The AHRQ analysis showed that in patients aged ≥ 12 years there was no significant difference between the intermittent versus the regular use of ICS as regards the effect on exacerbation risk, spirometry results, Asthma Control Questionnaire (ACQ) score, Asthma Quality of Life Questionnaire (AQLQ) score, or albuterol rescue use. In patients aged 5–11 years, there was insufficient evidence to draw conclusions on the impact of intermittent ICS versus ICS controller for all endpoints except for rescue albuterol use, where there was weak evidence showing no difference between the two strategies.

The Camargos 2018 trial assessed the efficacy of intermittent ICS in children and adolescents aged 6–18 years compared to continuous ICS and found that the amount of steroid used in the intermittent ICS group used was 60% of that used by the continuous ICS group, with no significant difference between the two groups in the rate of exacerbation or asthma control. The trial was too small, with short follow-up duration.

The overall results of the recent and earlier published literature suggest the following:

- The cumulative dose of ICS in the daily use regimen is significantly higher than that used in the intermittent symptom-based ICS regimen.
• There is insufficient evidence to determine that the intermittent symptom-based use of ICS has superior or equivalent benefits versus daily ICS use in patients with persistent asthma. The published literature shows no significant differences between the regimens in the frequency of asthma exacerbation, number of patients with exacerbations requiring the use of oral corticosteroids, emergency room visits, hospitalization, serious adverse events, total withdrawals, or withdrawals due to treatment failure. However, the published trials were not designed as equivalence trials, and the lack of significant differences in outcomes between intermittent and daily ICS does not necessarily indicate that they are equivalent.
• There is insufficient evidence to determine the long-term effects of intermittent ICS use on lung growth and lung function decline in patients with persistent asthma.

2. In children aged ≥ 5 years, adolescents, and adults with persistent asthma, what is the comparative safety and effectiveness of:

- ICS-LABA controller and quick relief versus ICS controller without LABA plus SABA as needed?
- ICS-LABA controller and quick relief versus ICS controller and LABA at the same ICS dose plus SABA as needed?
- ICS-LABA controller and quick relief versus ICS controller and LABA at a higher ICS dose plus SABA as needed?
- Off label use of ICS-LABA as needed versus SABA as needed?
- Off label use of ICS-LABA as needed versus daily low-dose ICS plus SABA as needed?

ICS-LABA controller and quick relief versus ICS controller with or without LABA

The overall results of the systematic review and meta-analysis conducted by Sobieraj and colleagues (both 2018) show the following:

- ICS-LABA controller and quick relief versus ICS controller
  - At the same comparative ICS dose: Low- to moderate-strength evidence from systematic reviews and meta-analyses of earlier published trials suggests that ICS-LABA controller and quick relief compared to ICS controller at the same comparative dose may reduce the risk of exacerbations as composite outcomes and all-cause death, improves FEV1, and reduces rescue medication inhalations per day.
  - At a higher comparative ICS dose: Low-strength evidence suggests that ICS-LABA controller and quick relief compared to ICS controller at a higher comparative ICS dose reduces the risk of exacerbations as composite outcomes in patients aged ≥ 12 years and in patients aged 4–11 years.

- ICS-LABA controller and quick relief versus ICS and LABA controller
  - At the same comparative ICS dose: Moderate- to high-strength evidence suggests that ICS-LABA controller and quick relief compared to ICS and LABA controller at the same comparative ICS dose reduces the composite rate of exacerbation requiring systemic corticosteroids, hospitalization, or emergency room visits in patients aged ≥ 12 years with symptomatic or uncontrolled asthma (persistence severity not described). The evidence for patients aged 4–11 years is of low strength due to the lack of trials.
  - At a higher comparative ICS dose: Strong evidence indicates that ICS-LABA controller and quick relief compared to ICS and LABA controller at a higher ICS dose reduces the risk of composite exacerbations in patients aged ≥12 years with no difference in death rates, ACQ-5 score, FEV1, Asthma Quality of Life Questionnaire (AQLQ)-(S) score, and rescue medication use. No evidence was found for patients aged 5–11 years.

As-needed ICS-LABA (budesonide-formoterol) (off-label use)

- Compared to SABA: Moderate- to high-quality evidence from recent RCTs suggests the following:
  - ICS-LABA as needed may have only a slight benefit compared to SABA alone in controlling asthma symptoms (O’Byrne 2018). (The same trial, SYGMA 1, also showed that ICS regular use was superior to SABA in reducing exacerbations.)
  - ICS-LABA used as needed may significantly reduce the number of exacerbations compared to SABA alone in the SYGMA 1 trial and in the Novel START trial (Beasley 2019). The latter was an open-label trial described as a real-life study.
  - Comparisons in these trials were among the GINA step II population, in which SABA alone is not indicated.
Compared to ICS daily use with SABA as needed
  - As-needed ICS-LABA was inferior (provided poorer asthma control) compared to ICS daily use with SABA as needed (O’Byrne 2018, Bateman 2018, Beasley 2019).
  - The effect of as-needed ICS-LABA compared to ICS with SABA as needed in preventing or reducing the rate of severe exacerbations varied slightly between the trials:
    - ICS-LABA was superior in preventing severe exacerbations in patients with mild asthma (Novel-START study) and mild to moderate asthma (Hardy 2019).
    - ICS-LABA was borderline superior in preventing severe exacerbations (Hardy 2019).
    - ICS-LABA was non-inferior to ICS in reducing the rate of severe exacerbations (Bateman 2018).
    - No significant difference was found between the two budesonide groups in the annual rate of severe exacerbations (those requiring systemic glucocorticoids) (O’Byrne 2018).
  - The median daily dose of inhaled glucocorticoid in the budesonide-formoterol group was less than or equal to one-quarter of the dose used in the regular budesonide group (O’Byrne 2018, Bateman 2018).

The overall results of the published studies on as-needed ICS-LABA use in patients with mild persistent asthma (mild to moderate in one study) suggest that as-needed ICS-LABA use:
- Has a minimal benefit in asthma control compared to SABA alone.
- Provides poorer asthma control compared to regular use of ICS with SABA as needed.
- Shows no significant difference (or minor improvement) compared to regular use of ICS with SABA as needed in reducing the rate of severe exacerbations in patients with mild persistent asthma (mild to moderate in one study).
- Considerably lowers the daily use of ICS compared to the regular daily use of ICS with SABA as needed.

The studies suggest that there is no significant difference in the adverse events between as-needed ICS-LABA and daily use of regular ICS.

No comparisons were made between ICS-LABA used as a controller and quick relief therapy versus ICS-LABA as needed with SABA as needed.

3. In children and adults with asthma, what is the comparative effectiveness and safety of combination ICS-formoterol versus ICS-salmeterol used as daily controller and quick relief therapy plus SABA as needed, in controlling symptoms, improving quality of life, and reducing the risk of asthma exacerbations, hospital admission, and mortality?
- The literature search did not identify any recently published large RCTs on the comparative efficacy and safety of regular use of fixed dose ICS-formoterol and ICS-salmeterol in patients with chronic asthma.
- There is good evidence from the earlier COMPASS study (Kuna 2007) showing that fixed-dose budesonide/formoterol is superior to salmeterol/fluticasone in reducing the rate of exacerbations requiring hospitalization/ER treatment in adolescents and adults with chronic asthma (NNT = 33 in 6 months).

4. What are the guidelines for managing asthma exacerbations in primary care and in an acute care facility?

The recommendations of the GINA and SIGN guidelines have been adopted.

5. Does the long-term use of ICS in children with persistent asthma have any influence on their linear growth, bone health, or adrenal suppression? If yes, is that effect dependent on the formulation type, dose, or duration of use? Is there any impact on final adult height?

The published studies and meta-analyses (e.g., Axelsson 2019, Loke 2015, Kwda 2019, Zhang 2014, Pruteanu 2014, Kelly 2012) provide low- to moderate-strength evidence suggesting that:
- The long-term use (12 months) of ICS is associated with a slight reduction in growth velocity and final adult height in children.
The reduction in growth velocity appeared to be most prominent in the first year of therapy (average 0.48 cm/year) and less significant at 24- or 36-month follow-up of prepubertal children with mild to moderate persistent asthma.

- Adverse effects on growth may be more prominent in younger children than in older children.
- The initial decrease in attained height related to ICS in prepubertal age may persist as a reduction in adult height.
- ICS-induced growth suppression may be dose-dependent, as lower doses of ICS were found to have less impact on growth than higher doses.
- Fluticasone may be associated with less suppressive effects compared to beclomethasone and budesonide in children with asthma.
- The ICS therapy delivery device may impact the effect size of ICS on growth.

The evidence, however, should be interpreted with caution: Accurate assessment of the effect of ICS on children's growth may be difficult. Growth is affected by several factors, including 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. Additionally, as the effect of ICS may vary according to the formulation used, delivery system or device may affect the consistency of dosing, effective dose delivered, adherence to therapy, and other factors.

Also, the majority of published studies included in the meta-analyses were published 10–20 years earlier, with many developments in asthma management and behavioral, environmental, and nutritional factors occurring in the meantime. The studies were mainly short-term and did not follow the patients long enough to assess the effect of ICS on final growth or to determine whether catch-up growth would allow them to reach their growth potential.

6. **What is the comparative safety and efficacy of SABA and ICS for exercise-induced bronchoconstriction (EIB) in children? Is there a threshold dose for the development of tachyphylaxis?**

- There is insufficient published evidence to determine a specific threshold dose for the development of tachyphylaxis with SABA in children. The American Thoracic Society 2013 guideline (Parsons 2013) recommends that, because the daily use of SABAs has been shown to lead to tolerance, they should be used for EIB prevention only intermittently (i.e., less than daily on average).
- There is insufficient published evidence to determine the comparative efficacy and safety of SABA and ICS for the prevention and/or control of symptoms in children with EIB.

7. **What is the comparative efficacy and safety of on-demand versus regular daily use of ICS in preventing/controlling symptoms of exercise-induced bronchospasm in children aged > 5 years?**

- There is insufficient evidence from recent RCTs that specifically examined the comparative effectiveness and safety of as-needed compared to regular daily use of ICS in controlling symptoms of EIB in children aged > 5 years.

8. **Is there an association between montelukast therapy and neuropsychiatric events in children with asthma? Should montelukast be used for exercise-induced bronchospasm in children?**

- The literature suggests that there may be an association between montelukast and neuropsychiatric events, but there is insufficient published evidence to determine whether it is a causal association. The published studies that examined this association were retrospective nested-case control studies, with the patient data obtained from prescription claims and administrative health care data. Two large case-control studies (Glockler-Lauf 2019, Ali 2015) had conflicting results: The Glockler-Lauf analysis of patient data in Canada showed that children who experienced a new-onset neuropsychiatric event had nearly twice the odds of having been prescribed montelukast, compared with controls. On the other hand, the Ali case-control retrospective analysis performed in the U.S. found no such association between montelukast and any neuropsychiatric event or psychiatric disorder diagnosis.
• There is low-strength evidence suggesting that LTRA with or without ICS may be effective in reducing EIB in some, but not all, children with or without asthma.

9. What strategies or interventions are effective in improving medication adherence, asthma control, and associated morbidity and mortality in minority groups including children and adults?

• Low- to moderate-strength evidence from small randomized and non-randomized observational studies and/or intervention programs (Apter 2019, Kapheim 2015, Marshall 2020, McCullum 2017, Naar 2018, Patel 2017, Press 2012) suggests that education programs (especially culture-specific) delivered by community health workers (most studied), nurses, or pharmacists may improve asthma control in minority groups, mainly African American and Hispanic children and adults with asthma.

References


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 February 2021.

Team

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

Clinician lead: Katie Paul, MD, MPH, Clinical Lead, Clinical Improvement & Prevention
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