


2020 FOCUSED UPDATES TO THE Asthma Management Guidelines


CLINICIAN'S GUIDE

PURPOSE

This Clinician's Guide summarizes the *2020 Focused Updates to the Asthma Management Guidelines: A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group* to help clinicians integrate the new recommendations into clinical care. The full 2020 Report, which is focused on selected topics rather than a complete revision of the 2007 *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma* (EPR-3), can be found at **nhlbi.nih.gov/asthmaguidelines.** This summary guide should be used in conjunction with the full report. The Guide is organized by the following topics:

- **Intermittent Inhaled Corticosteroids**
- **Long-Acting Muscarinic Antagonists**
- **Indoor Allergen Mitigation**
- **Immunotherapy in the Treatment of Allergic Asthma**
- **Fractional Exhaled Nitric Oxide Testing**
- **Bronchial Thermoplasty**

Multiple stakeholders contributed to the selection of topics for the update. The Agency for Healthcare Research and Quality's (AHRQ) Evidence-Based Practice Centers conducted systematic reviews on these topics, which were subsequently published and used by the Expert Panel Working Group (the Expert Panel) of the National Asthma Education and Prevention Program Coordinating Committee (NAEPPCC), coordinated by the National Heart, Lung, and Blood Institute, as a basis for the updates. The Expert Panel used GRADE (Grading of Recommendations Assessment, Development, and Evaluation), an internationally accepted framework, for determining the certainty of evidence and the direction and strength of recommendations based on the evidence. Each recommendation is described as either strong or conditional. For all recommendations, shared decision making should be used to help individuals with asthma make choices that are consistent with their risks, values, and preferences; this is especially important for conditional recommendations.

Diagrams showing the recommended approaches to care, including the new recommendations, for individuals with asthma based on age have been updated from EPR-3. Within a given step, the preferred options are the best management choices supported by the evidence reviewed by the Expert Panel. When the available evidence was insufficient or did not change a previous recommendation, the diagrams list the preferred options from EPR-3. The diagrams are meant to assist, and not replace, clinical judgment or decision making required for individual patient management with input from individuals with asthma about their preferences.

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INTERMITTENT INHALED CORTICOSTEROIDS

Scheduled, daily inhaled corticosteroid (ICS) treatment is the currently preferred pharmacologic controller therapy for persistent asthma in individuals of all ages. Intermittent ICS dosing includes courses of ICS treatment used for brief periods, usually in response to symptoms or as an add-on with or without a long-acting beta$_2$-agonist (LABA). Recommendations for ICS treatment are organized by age.

Children Ages 0–4 Years with Recurrent Wheezing

KEY POINT

In children ages 0–4 years with recurrent wheezing, a short (7–10 day) course of daily ICS with as-needed inhaled short-acting beta$_2$-agonist (SABA) for quick-relief therapy is recommended starting at the onset of a respiratory tract infection.

IMPLEMENTATION GUIDANCE AND CONSIDERATIONS FOR SHARED DECISION-MAKING

- **Target population:** Children ages 0–4 years with recurrent wheezing (at least three episodes of wheezing triggered by apparent infection in their lifetime or two episodes in the past year with no symptoms between infections) and who are not taking daily asthma treatment.
- **Treatment:** One regimen used in two reviewed studies is budesonide inhalation suspension, 1 mg twice daily for 7 days at the first sign of respiratory tract infection-associated symptoms.
- **Potential benefits:** The main benefit during respiratory tract infections is a reduction in exacerbations requiring systemic corticosteroids.
- **Potential risks:** This treatment could affect growth. Carefully monitor growth in children who use this treatment.
- **Other considerations:** Caregivers can initiate intermittent ICS treatment at home without a visit to a health care provider when they have clear instructions.

RECOMMENDATION

In children ages 0–4 years with recurrent wheezing triggered by respiratory tract infections and no wheezing between infections, the Expert Panel conditionally recommends starting a short course of daily ICS at the onset of a respiratory tract infection with as-needed SABA for quick-relief therapy compared to as-needed SABA for quick-relief therapy only.

Individuals Ages 4 Years and Older with Persistent Asthma

KEY POINTS

- For individuals with **mild to moderate** persistent asthma who are taking daily ICS treatment (likely adherent with prescribed daily ICS) as a controller, increasing the regular daily ICS dose for short periods is not recommended when symptoms increase or peak flow decreases.
- For individuals with **moderate to severe** persistent asthma already taking low- or medium-dose ICS, the preferred treatment is a single inhaler with ICS-formoterol (referred to as single maintenance and reliever therapy, or "SMART") used both daily and as needed.

Individuals Ages 12 Years and Older with Persistent Asthma

KEY POINTS

- For individuals with **mild** persistent asthma, either of the following two treatments are recommended as part of Step 2 therapy: 1) a daily low-dose ICS and as-needed SABA for quick-relief therapy, or 2) intermittent as-needed SABA and ICS used one after the other for worsening asthma.
  - ✓ One approach to intermittent therapy is 2–4 puffs of albuterol followed by 80–250 mcg of beclomethasone equivalent every 4 hours as needed for asthma symptoms.
  - ✓ Intermittent therapy can be initiated at home with regular provider follow-up to ensure that the intermittent regimen is still appropriate.
  - ✓ Individuals with either low or high perception of symptoms may not be good candidates for as-needed ICS therapy. Daily low-dose ICS with as-needed SABA may be preferred.
- For individuals with **moderate to severe** persistent asthma already taking low- or medium-dose ICS, the preferred treatment is a single inhaler with ICS-formoterol (referred to as single maintenance and reliever therapy, or "SMART") used both daily and as needed.

RECOMMENDATIONS (AGES 4+)

- In individuals ages 4 years and older with mild to moderate persistent asthma who are likely to be adherent to daily ICS treatment, the Expert Panel conditionally recommends against a short-term increase in the ICS dose for increased symptoms or decreased peak flow.
- In individuals ages 4 years and older with moderate to severe persistent asthma, the Expert Panel recommends ICS-formoterol in a single inhaler used as both daily controller and reliever therapy compared to either a higher-dose ICS as daily controller therapy and SABA for quick-relief therapy or the same-dose ICS-LABA as daily controller therapy and SABA for quick-relief therapy.

RECOMMENDATIONS (AGES 12+)

- In individuals ages 12 years and older with mild persistent asthma, the Expert Panel conditionally recommends either daily low-dose ICS and as-needed SABA for quick-relief therapy or as-needed ICS and SABA used concomitantly.
- In individuals ages 12 years and older with moderate to severe persistent asthma, the Expert Panel conditionally recommends ICS-formoterol in a single inhaler used as both daily controller and reliever therapy compared to higher-dose ICS-LABA as daily controller therapy and SABA for quick-relief therapy.

SINGLE MAINTENANCE AND RELIEVER THERAPY (SMART) IMPLEMENTATION GUIDANCE AND CONSIDERATIONS FOR SHARED DECISION MAKING

- **Target population:** Individuals 4 years and older with a severe exacerbation in the prior year are particularly good candidates for SMART to reduce exacerbations.
- **Who should not receive this treatment:** Do not use ICS-formoterol as reliever therapy in individuals taking ICS-salmeterol as maintenance therapy.
- **Treatment:** Inhaled ICS-formoterol in a single inhaler. This form of therapy has only been studied with formoterol as the long-acting beta$_2$-agonist (LABA).
  - ✓ SMART is appropriate for Step 3 (low-dose ICS) and Step 4 (medium-dose ICS) treatment.
  - ✓ Individuals whose asthma is uncontrolled on maintenance ICS-LABA with SABA as quick-relief therapy should receive the preferred SMART if possible before moving to a higher step of therapy.
  - ✓ ICS-formoterol should be administered as maintenance therapy with 1–2 puffs once or twice daily (depending on age, asthma severity, and ICS dose in the ICS-formoterol preparation) and 1–2 puffs as needed for asthma symptoms.
  - ✓ Maximum number of puffs per day is 8 (36 mcg formoterol) for children ages 4–11 years and 12 (54 mcg formoterol) for individuals ages 12 years and older.
  - ✓ Advise individuals to contact their physician if they need to exceed maximum number of puffs.
  - ✓ Dose of formoterol was based on 4.5 mcg/inhalation, the most common preparation used in the studies reviewed.
- **Potential benefits:** In studies this treatment consistently reduced asthma exacerbations requiring unscheduled medical visits or systemic corticosteroids and in some studies improved asthma control and quality of life. Reduced exposure to oral corticosteroids and to ICS treatment suggest that the intervention might reduce future corticosteroid-associated harms.
- **Potential risks:** Studies found no difference in documented harms between this type of therapy and daily ICS, or ICS-LABA, with SABA as quick relief therapy.
- **Other considerations:**
  - ✓ In children ages 4–11 years, there may be a lower risk of growth suppression among those taking SMART versus daily higher-dose ICS treatment.
  - ✓ This recommendation might not be appropriate for some individuals with asthma because of cost, formulary considerations, or medication intolerance.
  - ✓ A 1-month supply of ICS-formoterol medication that is sufficient for maintenance therapy may not last a month if the inhaler is used for reliever therapy as well.

LONG-ACTING MUSCARINIC ANTAGONISTS

Long-acting muscarinic antagonists (LAMAs)* comprise a pharmacologic class of long-acting bronchodilators.

Individuals Ages 12 Years and Older with Uncontrolled Persistent Asthma

KEY POINTS

- In individuals with asthma that is not controlled by ICS therapy alone, adding a LABA rather than a LAMA to an ICS is recommended.
- However, if a LABA cannot be used (unable to tolerate, contraindication, inability to use device, or the LABA is unavailable), adding a LAMA to an ICS is an acceptable alternative.
- For individuals whose asthma is not controlled with ICS-LABA, adding a LAMA is recommended for many individuals because it offers a small potential benefit.

IMPLEMENTATION GUIDANCE AND CONSIDERATIONS FOR SHARED DECISION MAKING

- **When to use treatment:** Prescribe this medication for long-term asthma control in the ambulatory setting.
- **Who should not receive this treatment:** Individuals at risk of urinary retention or those who have glaucoma.
- **Potential benefits:** The addition of a LAMA to ICS-LABA may improve asthma control and quality of life. The addition of a LAMA to an ICS provides a small potential benefit compared to continuing the same ICS dose if an individual cannot use a LABA for any reason.
- **Potential risks:** Adding a LAMA to ICS controller therapy provides no more benefit than adding a LABA to ICS controller therapy and may increase the risk of harm, based on a single real-world study in Blacks.
- **Other considerations:** Adding LAMA therapy to ICS-LABA requires the use of an additional and different type of inhaler. Teach individuals with asthma how to use these devices appropriately.

RECOMMENDATIONS

- In individuals ages 12 years and older with uncontrolled persistent asthma, the Expert Panel conditionally recommends against adding LAMA to ICS compared to adding LABA to ICS.
- If LABA is not used in individuals ages 12 years and older with uncontrolled persistent asthma, the Expert Panel conditionally recommends adding LAMA to ICS controller therapy compared to continuing the same dose of ICS alone.
- In individuals ages 12 years and older with uncontrolled persistent asthma, the Expert Panel conditionally recommends adding LAMA to ICS-LABA compared to continuing the same dose of ICS-LABA.

*At the time of this writing, tiotropium bromide (RESPIMAT®) was the only formulation of LAMA with U.S. Food and Drug Administration (FDA) approval for asthma treatment.

INDOOR ALLERGEN MITIGATION

In some individuals, asthma can have an allergic component. Allergen mitigation strategies (e.g., air purifiers, impermeable pillow and mattress covers, HEPA filters) aim to decrease an individual's exposure to allergens.

KEY POINTS

- Overall, the studies reviewed provided little evidence that allergen mitigation strategies are beneficial for improving asthma outcomes.
- For individuals with asthma with an allergy to a specific indoor substance (e.g., dust mites), using multiple strategies to reduce the allergen is recommended, since using only one strategy often does not improve asthma outcomes.
- Integrated pest management in the home is recommended for individuals with asthma who are allergic and exposed to cockroaches or rodents (e.g., mice).
- For individuals with asthma who do not have allergies to indoor substances, environmental interventions in the home are not recommended.

IMPLEMENTATION GUIDANCE AND CONSIDERATIONS FOR SHARED DECISION-MAKING

- Consider allergen testing, when appropriate (based on clinical history and exposures) and feasible, before committing individuals to specific allergen mitigation strategies that may be burdensome.
- Consider the severity of an individual's asthma, the small benefit, and the extent of previous symptoms and exacerbations when recommending allergen mitigation interventions.
- Allergen mitigation interventions may be expensive or difficult for individuals to use or maintain.

RECOMMENDATIONS

- In individuals with asthma who have symptoms related to exposure to identified indoor allergens, confirmed by history taking or allergy testing, the Expert Panel conditionally recommends a multi-component allergen-specific mitigation intervention.
- In individuals with asthma who have sensitization or symptoms related to exposure to dust mites, the Expert Panel conditionally recommends impermeable pillow/mattress covers only as part of a multicomponent allergen mitigation intervention, not as a single-component intervention.
- In individuals with asthma who have sensitization or symptoms related to exposure to pests (cockroaches and rodents), the Expert Panel conditionally recommends the use of integrated pest management alone, or as part of a multicomponent allergen-specific mitigation intervention.
- In individuals with asthma who do not have sensitization to specific indoor allergens or who do not have symptoms related to exposure to specific indoor allergens, the Expert Panel conditionally recommends *against* allergen mitigation interventions as part of routine asthma management.

IMMUNOTHERAPY IN THE TREATMENT OF ALLERGIC ASTHMA

Immunotherapy is the administration of an aeroallergen either subcutaneously (subcutaneous immunotherapy [SCIT]) or sublingually (sublingual immunotherapy [SLIT] in the form of aqueous drops or tablets).

Subcutaneous Immunotherapy

KEY POINTS

- SCIT is recommended as an adjunct treatment for individuals who have demonstrated allergic sensitization and evidence of worsening asthma symptoms after exposure to the relevant antigen or antigens.
- Do not initiate, increase, or administer maintenance SCIT doses while individuals have asthma symptoms or to individuals with severe asthma.

IMPLEMENTATION GUIDANCE AND CONSIDERATIONS FOR SHARED DECISION MAKING

- Administer SCIT in a clinical setting and provide direct supervision and observation for at least 30 minutes because of the risk of systemic reactions. Individuals with asthma should not administer SCIT at home.
- Delayed systemic reactions (those occurring more than 30 minutes after injection) occur in approximately 15 percent of individuals after injection.
- Individuals who have had previous clinically significant reactions to immunotherapy should bring injectable epinephrine to and from the clinic on the day of their injection.

RECOMMENDATION

In individuals ages 5 years and older with mild to moderate allergic asthma, the Expert Panel conditionally recommends the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in those individuals whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy.

Sublingual Immunotherapy

KEY POINT

The evidence reviewed did not support the use of SLIT specifically for the treatment of allergic asthma.

RECOMMENDATION

In individuals with persistent allergic asthma, the Expert Panel conditionally recommends against the use of sublingual immunotherapy in asthma treatment.

FRACTIONAL EXHALED NITRIC OXIDE TESTING

Nitric oxide can be measured in exhaled breath and can serve as a measure of the level of airway inflammation. In individuals with asthma, fractional exhaled nitric oxide (FeNO) may be a useful indicator of type 2 (T2) inflammation in the airway.

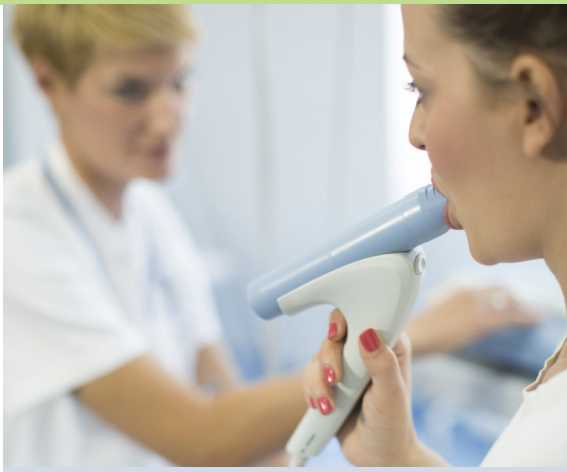
FeNO Testing in the Diagnosis of Asthma

KEY POINTS

- FeNO measurement may support a diagnosis of asthma in individuals for whom the diagnosis is uncertain, even after a complete history, physical examination, and spirometry testing including bronchodilator responsiveness.
- In children ages 4 years and younger who have recurrent episodes of wheezing, FeNO measurement does not reliably predict the future development of asthma.

IMPLEMENTATION GUIDANCE AND CONSIDERATIONS FOR SHARED DECISION MAKING

- FeNO levels greater than 50 ppb (or greater than 35 ppb in children ages 5–12 years) are consistent with elevated T2 inflammation and support a diagnosis of asthma.
- Allergic rhinitis and atopy, which can be present in individuals with and without asthma, are associated with increased FeNO levels. Taking these factors into consideration is critical for accurately interpreting FeNO test results.



RECOMMENDATIONS

- In children ages 0–4 years with recurrent wheezing, the Expert Panel recommends against FeNO measurement to predict the future development of asthma.
- In individuals ages 5 years and older for whom the diagnosis of asthma is uncertain using history, clinical findings, clinical course, and spirometry, including bronchodilator responsiveness testing, or in whom spirometry cannot be performed, the Expert Panel conditionally recommends the addition of FeNO measurement as an adjunct to the evaluation process.

FeNO Testing in the Management of Asthma in Individuals Ages 5 Years and Older

KEY POINTS

- FeNO testing should not be used in isolation to assess asthma control, predict a future asthma exacerbation, or assess the severity of an exacerbation.
- FeNO measurement may be used in conjunction with an individual's history, clinical findings, and spirometry as part of an ongoing asthma monitoring and management strategy which includes frequent FeNO assessments.

IMPLEMENTATION GUIDANCE AND CONSIDERATIONS FOR SHARED DECISION MAKING

- Interpret FeNO levels in conjunction with other clinical data because these levels are affected by comorbid conditions, including allergic rhinitis and atopy, or behaviors such as smoking.
- Cutpoints for adjusting therapy to reduce the risk of exacerbation have not been established.

RECOMMENDATIONS

- In individuals ages 5 years and older with persistent allergic asthma, for whom there is uncertainty in choosing, monitoring, or adjusting anti-inflammatory therapies based on history, clinical findings, and spirometry, the Expert Panel conditionally recommends the addition of FeNO measurement as part of an ongoing asthma monitoring and management strategy that includes frequent assessments.
- In individuals ages 5 years and older with asthma, the Expert Panel recommends against the use of FeNO measurements in isolation to assess asthma control, predict future exacerbations, or assess exacerbation severity. If used, it should be as part of an ongoing monitoring and management strategy.

BRONCHIAL THERMOPLASTY

Bronchial thermoplasty (BT), a procedure that uses heat to remove muscle tissue from the airways of adults with moderate to severe asthma, was developed over the last decade.

KEY POINTS

- Most individuals ages 18 years and older with uncontrolled, moderate to severe, persistent asthma should not undergo BT to treat asthma because the benefits are small, the risks are moderate, and the long-term outcomes are uncertain.
- Some individuals with moderate to severe persistent asthma who have troublesome symptoms may be willing to accept the risks of BT and, therefore, might choose this intervention after shared decision making with their health care provider.

IMPLEMENTATION GUIDANCE AND CONSIDERATIONS FOR SHARED DECISION MAKING

- BT may reduce severe asthma exacerbations compared with standard care after treatment. Although the benefits could last 5 years or more, only limited data demonstrate that this treatment improves long-term asthma outcomes.
- The risks of BT include asthma exacerbations, hemoptysis, and atelectasis during the treatment period. In addition, severe, delayed-onset complications could occur that have not yet been recognized because of the small numbers of individuals who have undergone the procedure.
- Offer the procedure in the setting of a clinical trial or a registry study to enable the collection of long-term data on the use of BT for asthma.
- For individuals who decide to undergo BT, an experienced specialist (e.g., a pulmonologist with training in BT administration) should provide this treatment in a center that has appropriate expertise.
- BT has not been studied in individuals younger than age 18 years.

RECOMMENDATIONS

- In individuals ages 18 years and older with persistent asthma, the Expert Panel conditionally recommends *against* bronchial thermoplasty.
- Individuals ages 18 years and older with persistent asthma who place a low value on harms (short-term worsening symptoms and unknown long-term side effects) and a high value on potential benefits (improvement in quality of life, a small reduction in exacerbations) might consider bronchial thermoplasty.

AGES 0–4 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 0–4 Years				
Treatment	**STEP 1**	**STEP 2**	**STEP 3**	**STEP 4**	**STEP 5**	**STEP 6**
Preferred	PRN SABA and At the start of RTI: Add short course daily ICS▲	Daily low-dose ICS and PRN SABA	Daily low-dose ICS-LABA and PRN SABA▲ or Daily low-dose ICS + montelukast,* or daily medium-dose ICS, and PRN SABA	Daily medium-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA
Alternative		Daily montelukast* or Cromolyn,* and PRN SABA		Daily medium-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast*+ oral systemic corticosteroid and PRN SABA
			For children age 4 years only, see Step 3 and Step 4 on Management of Persistent Asthma in Individuals Ages 5–11 Years diagram.			

Assess Control

- First check adherence, inhaler technique, environmental factors,▲ and comorbid conditions.
- **Step up** if needed; reassess in 4–6 weeks
- **Step down** if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 3 or higher is required. Consider consultation at Step 2.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; SABA, inhaled short-acting beta$_2$-agonist; RTI, respiratory tract infection; PRN, as needed

▲ Updated based on the 2020 guidelines.

* Cromolyn and montelukast were not considered for this update and/or have limited availability for use in the United States. The FDA issued a Boxed Warning for montelukast in March 2020.

NOTES FOR INDIVIDUALS AGES 0–4 YEARS DIAGRAM

Quick-relief medications	• Use SABA as needed for symptoms. The intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. • **Caution:** Increasing use of SABA or use >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and may require a step up in treatment. • Consider short course of oral systemic corticosteroid if exacerbation is severe or individual has history of previous severe exacerbations.
Each step: Assess environmental factors, provide patient education, and manage comorbidities▲	• In individuals with sensitization (or symptoms) related to exposure to pests‡: conditionally recommend integrated pest management as a single or multicomponent allergen-specific mitigation intervention.▲ • In individuals with sensitization (or symptoms) related to exposure to identified indoor allergens, conditionally recommend a multi-component allergen-specific mitigation strategy.▲ • In individuals with sensitization (or symptoms) related to exposure to dust mites, conditionally recommend impermeable pillow/mattress covers only as part of a multicomponent allergen-specific mitigation intervention, but not as a single component intervention.▲
Notes	• If clear benefit is not observed within 4–6 weeks and the medication technique and adherence are satisfactory, the clinician should consider adjusting therapy or alternative diagnoses.
Abbreviations	EIB, exercise-induced bronchoconstriction; SABA, inhaled short-acting beta$_2$-agonist. ▲Updated based on the 2020 guidelines. ‡ Refers to mice and cockroaches, which were specifically examined in the Agency for Healthcare Research and Quality systematic review.

AGES 5–11 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 5–11 Years				
Treatment	**STEP 1**	**STEP 2**	**STEP 3**	**STEP 4**	**STEP 5**	**STEP 6**
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA	Daily and PRN combination low-dose ICS-formoterol▲	Daily and PRN combination medium-dose ICS-formoterol▲	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA
Alternative		Daily LTRA,* or Cromolyn,* or Nedocromil,* or Theophylline,* and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LTRA,* or daily low-dose ICS +Theophylline,* and PRN SABA	Daily medium-dose ICS-LABA and PRN SABA or Daily medium-dose ICS + LTRA* or daily medium-dose ICS + Theophylline,* and PRN SABA	Daily high-dose ICS + LTRA* or daily high-dose ICS + Theophylline,* and PRN SABA	Daily high-dose ICS + LTRA* + oral systemic corticosteroid or daily high-dose ICS + Theophylline* + oral systemic corticosteroid, and PRN SABA
		Steps 2–4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy▲			Consider Omalizumab**▲	

Assess Control

- First check adherence, inhaler technique, environmental factors,▲ and comorbid conditions.
- **Step up** if needed; reassess in 2–6 weeks
- **Step down** if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 3.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta$_2$-agonist

▲ Updated based on the 2020 guidelines.

* Cromolyn, Nedocromil, LTRAs including montelukast, and Theophylline were not considered in this update and/or have limited availability for use in the United States, and/or have an increased risk of adverse consequences and need for monitoring that make their use less desirable. The FDA issued a Boxed Warning for montelukast in March 2020.

** Omalizumab is the only asthma biologic currently FDA-approved for this age range.

NOTES FOR INDIVIDUALS AGES 5–11 YEARS DIAGRAM

Quick-relief medications	• Use SABA as needed for symptoms. The intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. • In Steps 3 and 4, the preferred option includes the use of ICS-formoterol 1 to 2 puffs as needed up to a maximum total daily maintenance and rescue dose of 8 puffs (36 mcg).▲ • **Caution:** Increasing use of SABA or use >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and may require a step up in treatment.
Each step: Assess environmental factors, provide patient education, and manage comorbidities▲	• In individuals with sensitization (or symptoms) related to exposure to pests‡: conditionally recommend integrated pest management as a single or multicomponent allergen-specific mitigation intervention.▲ • In individuals with sensitization (or symptoms) related to exposure to identified indoor allergens, conditionally recommend a multi-component allergen-specific mitigation strategy.▲ • In individuals with sensitization (or symptoms) related to exposure to dust mites, conditionally recommend impermeable pillow/mattress covers only as part of a multicomponent allergen-specific mitigation intervention, but not as a single component intervention.▲
Notes	• The terms ICS-LABA and ICS-formoterol indicate combination therapy with both an ICS and a LABA, usually and preferably in a single inhaler. • Where formoterol is specified in the steps, it is because the evidence is based on studies specific to formoterol. • In individuals ages 5–11 years with persistent allergic asthma in which there is uncertainty in choosing, monitoring, or adjusting anti-inflammatory therapies based on history, clinical findings, and spirometry, FeNO measurement is conditionally recommended as part of an ongoing asthma monitoring and management strategy that includes frequent assessment.
Abbreviations	EIB (exercise-induced bronchoconstriction); FeNO (fractional exhaled nitric oxide); ICS (inhaled corticosteroid); LABA (long-acting $beta_2$-agonist); SABA (inhaled short-acting $beta_2$-agonist). ▲Updated based on the 2020 guidelines. ‡ Refers to mice and cockroaches, which were specifically examined in the Agency for Healthcare Research and Quality systematic review.

AGES 12+ YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 12+ Years				
Treatment	**STEP 1**	**STEP 2**	**STEP 3**	**STEP 4**	**STEP 5**	**STEP 6** ■
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA or PRN concomitant ICS and SABA▲	Daily and PRN combination low-dose ICS-formoterol▲	Daily and PRN combination medium-dose ICS-formoterol▲	Daily medium-high dose ICS-LABA + LAMA and PRN SABA▲	Daily high-dose ICS-LABA + oral systemic corticosteroids + PRN SABA
Alternative		Daily LTRA* and PRN SABA or Cromolyn,* or Nedocromil,* or Zileuton,* or Theophylline,* and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LAMA,▲ or daily low-dose ICS + LTRA,* and PRN SABA or Daily low-dose ICS + Theophylline* or Zileuton,* and PRN SABA	Daily medium-dose ICS-LABA or daily medium-dose ICS + LAMA, and PRN SABA▲ or Daily medium-dose ICS + LTRA,* or daily medium-dose ICS + Theophylline,* or daily medium-dose ICS + Zileuton,* and PRN SABA	Daily medium-high dose ICS-LABA or daily high-dose ICS + LTRA,* and PRN SABA	
		Steps 2–4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy▲			Consider adding Asthma Biologics (e.g., anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13)**	

Assess Control

- First check adherence, inhaler technique, environmental factors,▲ and comorbid conditions.
- **Step up** if needed; reassess in 2–6 weeks
- **Step down** if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 3.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; LAMA, long-acting muscarinic antagonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta$_2$-agonist

▲ Updated based on the 2020 guidelines.

* Cromolyn, Nedocromil, LTRAs including Zileuton and montelukast, and Theophylline were not considered for this update, and/or have limited availability for use in the United States, and/or have an increased risk of adverse consequences and need for monitoring that make their use less desirable. The FDA issued a Boxed Warning for montelukast in March 2020.

** The AHRQ systematic reviews that informed this report did not include studies that examined the role of asthma biologics (e.g. anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13). Thus, this report does not contain specific recommendations for the use of biologics in asthma in Steps 5 and 6.

■ Data on the use of LAMA therapy in individuals with severe persistent asthma (Step 6) were not included in the AHRQ systematic review and thus no recommendation is made.

NOTES FOR INDIVIDUALS AGES 12+ YEARS DIAGRAM

Quick-relief medications	• Use SABA as needed for symptoms. The intensity of treatment depends on the severity of symptoms: up to 3 treatments at 20-minute intervals as needed. • In steps 3 and 4, the preferred option includes the use of ICS-formoterol 1 to 2 puffs as needed up to a maximum total daily maintenance and rescue dose of 12 puffs (54 mcg).▲ • **Caution:** Increasing use of SABA or use >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and may require a step up in treatment.
Each step: Assess environmental factors, provide patient education, and manage comorbidities▲	• In individuals with sensitization (or symptoms) related to exposure to pests‡: conditionally recommend integrated pest management as a single or multicomponent allergen-specific mitigation intervention.▲ • In individuals with sensitization (or symptoms) related to exposure to identified indoor allergens, conditionally recommend a multi-component allergen-specific mitigation strategy.▲ • In individuals with sensitization (or symptoms) related to exposure to dust mites, conditionally recommend impermeable pillow/mattress covers only as part of a multicomponent allergen-specific mitigation intervention, but not as a single component intervention.▲
Notes	• The terms ICS-LABA and ICS-formoterol indicate combination therapy with both an ICS and a LABA, usually and preferably in a single inhaler. • Where formoterol is specified in the steps, it is because the evidence is based on studies specific to formoterol. • In individuals ages 12 years and older with persistent allergic asthma in which there is uncertainty in choosing, monitoring, or adjusting anti-inflammatory therapies based on history, clinical findings, and spirometry, FeNO measurement is conditionally recommended as part of an ongoing asthma monitoring and management strategy that includes frequent assessment. • Bronchial thermoplasty was evaluated in Step 6. The outcome was a conditional recommendation against the therapy.
Abbreviations	EIB, exercise-induced bronchoconstriction; FeNO, fractional exhaled nitric oxide; ICS, inhaled corticosteroid; LABA, long-acting $beta_2$-agonist; SABA, inhaled short-acting $beta_2$-agonist. ▲Updated based on the 2020 guidelines. ‡ Refers to mice and cockroaches, which were specifically examined in the Agency for Healthcare Research and Quality systematic review.

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