



## Complete Summary

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### GUIDELINE TITLE

Medications: Expert panel report 3: guidelines for the diagnosis and management of asthma.

### BIBLIOGRAPHIC SOURCE(S)

Medications. In: National Asthma Education and Prevention Program (NAEPP). Expert panel report 3: guidelines for the diagnosis and management of asthma. Bethesda (MD): National Heart, Lung, and Blood Institute; 2007 Aug. p. 213-76. [315 references]

### GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: National Asthma Education and Prevention Program Expert Panel Report: guidelines for the diagnosis and management of asthma update on selected topics-2002. J Allergy Clin Immunol 2002 Nov;110(5 pt 2):S141-219.

### \*\* REGULATORY ALERT \*\*

### FDA WARNING/REGULATORY ALERT

**Note from the National Guideline Clearinghouse:** This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [February 21, 2007, Xolair \(Omalizumab\)](#): New reports of serious and life-threatening allergic reactions (anaphylaxis) in patients after treatment with Xolair.

### COMPLETE SUMMARY CONTENT

\*\* REGULATORY ALERT \*\*  
SCOPE  
METHODOLOGY - including Rating Scheme and Cost Analysis  
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IMPLEMENTATION OF THE GUIDELINE  
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

## SCOPE

### **DISEASE/CONDITION(S)**

Asthma

### **GUIDELINE CATEGORY**

Management  
Treatment

### **CLINICAL SPECIALTY**

Allergy and Immunology  
Emergency Medicine  
Family Practice  
Internal Medicine  
Pediatrics  
Pharmacology  
Preventive Medicine  
Pulmonary Medicine

### **INTENDED USERS**

Advanced Practice Nurses  
Allied Health Personnel  
Health Plans  
Nurses  
Physician Assistants  
Physicians  
Respiratory Care Practitioners

### **GUIDELINE OBJECTIVE(S)**

- To present recommendations for the diagnosis and management of asthma that will help clinicians and patients make appropriate decisions about asthma care
- To develop clinical practice tools and educational materials for patients and the public
- To revise the National Asthma Education and Prevention Program Expert Panel Report-2 Stepwise Approach for Managing Asthma in order to incorporate findings from the review of the scientific evidence
- To present an overview of asthma medications—both long-term control and quick-relief—and an overview of complementary alternative medicine strategies

### **TARGET POPULATION**

Infants, children, adolescents, and adults with asthma

## **INTERVENTIONS AND PRACTICES CONSIDERED**

### **Pharmacologic**

1. Long-term control medications
  - Corticosteroids (inhaled and systemic)
  - Cromolyn sodium and nedocromil
  - Immunomodulators
  - Leukotriene modifiers
  - Long-acting beta<sub>2</sub>-agonist(s)
  - Methylxanthines
2. Quick-relief medications
  - Anticholinergics
  - Short-acting beta<sub>2</sub>-agonist(s)
  - Systemic corticosteroids

### **Complementary and Alternative Medicine (Considered but Not Recommended)**

1. Acupuncture
2. Chiropractic therapy
3. Homeopathy and herbal medicine
4. Breathing techniques
5. Relaxation techniques
6. Yoga

## **MAJOR OUTCOMES CONSIDERED**

- Lung function measurements
  - Forced expiratory volume in one second (FEV<sub>1</sub>)
  - Peak expiratory flow (PEF)
- Symptom control as indicated by:
  - Symptom scores
  - Symptom frequency
  - Use of acute bronchodilator medication
  - Exacerbations
  - Use of oral corticosteroids
- Adverse effects of medications

## **METHODOLOGY**

### **METHODS USED TO COLLECT/SELECT EVIDENCE**

Hand-searches of Published Literature (Primary Sources)  
Searches of Electronic Databases

### **DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE**

In October 2004, the Expert Panel assembled for its first meeting. Using the Expert Panel Report (EPR)—2 1997 and EPR—Update 2002 as the framework, the Expert Panel organized the literature searches and subsequent report around the four essential components of asthma care, namely: (1) assessment and monitoring, (2) patient education, (3) control of factors contributing to asthma severity, and (4) pharmacologic treatment. Subtopics were developed for each of these four broad categories.

### **Inclusion/Exclusion Criteria**

The literature review was conducted in three cycles over an 18-month period (September 2004 to March 2006). Search strategies for the literature review initially were designed to cast a wide net but later were refined by using publication type limits and additional terms to produce results that more closely matched the framework of topics and subtopics selected by the Expert Panel. The searches included human studies with abstracts that were published in English in peer-reviewed medical journals in the MEDLINE database. Two timeframes were used for the searches, dependent on topic: January 1, 2001, through March 15, 2006, for pharmacotherapy (medications), peak flow monitoring, and written action plans, because these topics were recently reviewed in the EPR—Update 2002; and January 1, 1997, through March 15, 2006, for all other topics, because these topics were last reviewed in the EPR—2 1997.

### **Search Strategies**

Panel members identified, with input from a librarian, key text words for each of the four components of care. A separate search strategy was developed for each of the four components and various key subtopics when deemed appropriate. The key text words and Medical Subject Headings (MeSH) terms that were used to develop each search string are found in an appendix posted on the National Heart, Lung, and Blood Institute (NHLBI) Web site.

### **Literature Review Process**

The systematic review covered a wide range of topics. Although the overarching framework for the review was based on the four essential components of asthma care, multiple subtopics were associated with each component. To organize a review of such an expanse, the Panel was divided into 10 committees, with about 4 to 7 reviewers in each (all reviewers were assigned to 2 or more committees). Within each committee, teams of two ("topic teams") were assigned as leads to cover specific topics. A system of independent review and vote by each of the two team reviewers was used at each step of the literature review process to identify studies to include in the guidelines update. The initial step in the literature review process was to screen titles from the searches for relevancy in updating content of the guidelines, followed by reviews of abstracts of the relevant titles to identify those studies meriting full-text review based on relevance to the guidelines and study quality.

The combined number of titles screened from cycles 1, 2, and 3 was 15,444. The number of abstracts and articles reviewed for all three cycles was 4,747. Of these, 2,863 were voted to the abstract Keep list following the abstract-review step. A database of these abstracts is posted on the NHLBI Web site. Of these abstracts,

2,122 were advanced for full-text review, which resulted in 1,654 articles serving as a bibliography of references used to update the guidelines, available on the NHLBI Web site. Articles were selected from this bibliography for evidence tables and/or citation in the text. In addition, articles reporting new and particularly relevant findings and published after March 2006 were identified by Panel members during the writing period (March 2006–December 2006) and by comments received from the public review in February 2007.

## **NUMBER OF SOURCE DOCUMENTS**

Not stated

## **METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE**

Weighting According to a Rating Scheme (Scheme Given)

## **RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE**

The system\* used to describe the level of evidence is as follows:

### **Evidence Category A: Randomized controlled trials (RCTs), rich body of data.**

Evidence is from end points of well-designed RCTs that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.

### **Evidence Category B: RCTs, limited body of data.**

Evidence is from end points of intervention studies that include only a limited number of patients, post hoc or subgroup analysis of RCTs, or meta-analysis of RCTs. In general, category B pertains when few randomized trials exist; they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.

### **Evidence Category C: Nonrandomized trials and observational studies.**

Evidence is from outcomes of uncontrolled or nonrandomized trials or from observational studies.

### **Evidence Category D: Panel consensus judgment.**

This category is used only in cases where the provision of some guidance was deemed valuable, but the clinical literature addressing the subject was insufficient to justify placement in one of the other categories. The Panel consensus is based on clinical experience or knowledge that does not meet the criteria for categories A through C.

\*Source: Jadad AR, Moher M, Browman GP, Booker L, Sigouin C, Fuentes M, Stevens R. Systematic reviews and meta-analyses on treatment of asthma: critical evaluation. *BMJ* 2000;320(7234):537-40.

## **METHODS USED TO ANALYZE THE EVIDENCE**

## **DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE**

### **Preparation of Evidence Tables**

Evidence tables were prepared for selected topics. It was not feasible to generate evidence tables for every topic in the guidelines. Furthermore, many topics did not have a sufficient body of evidence or a sufficient number of high-quality studies to warrant the preparation of a table. The Panel decided to prepare evidence tables on those topics for which an evidence table would be particularly useful to assess the weight of the evidence—e.g., topics with numerous articles, conflicting evidence, or which addressed questions raised frequently by clinicians. Summary findings on topics without evidence tables, however, also are included in the updated guidelines text. Evidence tables were prepared with the assistance of a methodologist who served as a consultant to the Expert Panel. Within their respective committees, Expert Panel members selected the topics and articles for evidence tables. The evidence tables included all articles that received a "yes" vote from both the primary and secondary reviewer during the systematic literature review process. The methodologist abstracted the articles to the tables, using a template developed by the Expert Panel. The Expert Panel subsequently reviewed and approved the final evidence tables. A total of 20 tables, comprising 316 articles are included in the current update. Evidence tables are posted on the National Heart, Lung, and Blood Institute (NHLBI) Web site.

### **Ranking the Evidence**

The Expert Panel agreed to specify the level of evidence used to justify the recommendations being made. Panel members only included ranking of evidence for recommendations they made based on the scientific literature in the current evidence review. They did not assign evidence rankings to recommendations pulled through from the Expert Panel Report (EPR)—2 1997 on topics that are still important to the diagnosis and management of asthma but for which there was little new published literature. These "pull through" recommendations are designated by EPR—2 1997 in parentheses following the first mention of the recommendation. For recommendations that have been either revised or further substantiated on the basis of the evidence review conducted for the EPR—3: Full Report 2007, the level of evidence is indicated in the text in parentheses following first mention of the recommendation. Refer to the "Rating Scheme for the Strength of the Evidence" for the system used to describe the level of evidence.

## **METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Expert Consensus

## **DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

The steps used to develop this report include: (1) completing a comprehensive search of the literature; (2) conducting an in-depth review of relevant abstracts

and articles; (3) preparing evidence tables to assess the weight of current evidence with respect to past recommendations and new and unresolved issues; (4) conducting thoughtful discussion and interpretation of findings; (5) ranking strength of evidence underlying the current recommendations that are made; (6) updating text, tables, figures, and references of the existing guidelines with new findings from the evidence review; (7) circulating a draft of the updated guidelines through several layers of external review, as well as posting it on the National Heart, Lung, and Blood Institute (NHLBI) Web site for review and comment by the public and the National Asthma Education and Prevention Program Coordinating Committee (NAEPP CC), and (8) preparing a final-report based on consideration of comments raised in the review cycle.

### **Panel Discussion**

The first opportunity for discussion of findings occurred within the "topic teams." Teams then presented a summary of their findings during a conference call to all members of their respective committee. A full discussion ensued on each topic, and the committee arrived at a consensus position. Teams then presented their findings and the committee position to the full Expert Panel at an in-person meeting, thereby engaging all Panel members in critical analysis of the evidence and interpretation of the data. A series of conference calls for each of the 10 committees as well as four in-person Expert Panel meetings (held in October 2004, April 2005, December 2005, and May 2006) were scheduled to facilitate discussion of findings and to dovetail with the three cycles of literature review that occurred over the 18-month period. Potential conflicts of interest were disclosed at the initial meeting.

### **Report Preparation**

Development of the Expert Panel Report (EPR)—3: Full Report 2007 was an iterative process of interpreting the evidence, drafting summary statements, and reviewing comments from the various external reviews before completing the final report. In the summer and fall of 2005, the various topic teams, through conference calls and subsequent electronic mail, began drafting their assigned sections of the report. Members of the respective committees reviewed and revised team drafts, also by using conference calls and electronic mail. During the calls, votes were taken to ensure agreement with final conclusions and recommendations.

During the December 2005 meeting, Panel members reviewed and discussed all committee drafts. During the May 2006 meeting, the Panel conducted a thorough review and discussion of the report and reached consensus on the recommendations. For controversial topics, votes were taken to ensure that each individual's opinion was considered.

### **RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS**

In addition to specifying the level of evidence supporting a recommendation, the Expert Panel agreed to indicate the strength of the recommendation. When a certain clinical practice "is recommended," this indicates a strong recommendation by the panel. When a certain clinical practice "should, or may, be considered," this indicates that the recommendation is less strong.

This distinction is an effort to address nuances of using evidence ranking systems. For example, a recommendation for which clinical randomized controlled trial data are not available (e.g., conducting a medical history for symptoms suggestive of asthma) may still be strongly supported by the Panel. Furthermore, the range of evidence that qualifies a definition of "B" or "C" is wide, and the Expert Panel considered this range and the potential implications of a recommendation as they decided how strongly the recommendation should be presented.

## **COST ANALYSIS**

A formal cost analysis was not performed and published cost analyses were not reviewed.

## **METHOD OF GUIDELINE VALIDATION**

Peer Review

## **DESCRIPTION OF METHOD OF GUIDELINE VALIDATION**

In July, using conference calls and electronic mail, the Panel completed a draft of the Expert Panel Report (EPR)—3: Full Report 2007 for submission in July/August to a panel of expert consultants for their review and comments. In response to their comments, a revised draft of the EPR—3: Full Report 2007 was developed and circulated in November to the National Asthma Education and Prevention Program (NAEPP) Guidelines Implementation Panel (GIP) for their comment. This draft was also posted on the National Heart Lung and Blood Institute (NHLBI) Web site for public comment in February 2007. The Expert Panel considered 721 comments from 140 reviewers. Edits were made to the documents, as appropriate, before the full EPR—3: Full Report 2007 was finalized and published.

# **RECOMMENDATIONS**

## **MAJOR RECOMMENDATIONS**

Definitions of the levels of the evidence (A, B, C, D) and strength of recommendations ("is recommended" and "should or may, be considered") are presented at the end of the "Major Recommendations" field.

**Note from the National Asthma Education and Prevention Program (NAEPP):** Panel members only included ranking of evidence for recommendations they made based on the scientific literature in the current evidence review. They did not assign evidence rankings to recommendations pulled through from the Expert Panel Report (EPR)—2 1997 on topics that are still important to the diagnosis and management of asthma but for which there was little new published literature. These "pull through" recommendations are designated by EPR—2 1997 in parentheses following the first mention of the recommendation.

**Note from the NAEPP and the National Guideline Clearinghouse (NGC):** The Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma have been divided into individual summaries covering assessment,

education, medications, and management. In addition to the current summary, the following are available:

- [Measures of asthma assessment and monitoring.](#)
- [Education for a partnership in asthma care.](#)
- [Control of environmental factors and comorbid conditions that affect asthma.](#)
- [Managing asthma long term in children 0-4 years of age and 5-11 years of age.](#)
- [Managing asthma long term in youths >12 years of age and adults.](#)
- [Managing asthma long term—special situations](#)
- [Managing exacerbations of asthma.](#)

### **Key Points: Medications**

Medications for asthma are categorized into two general classes: long-term control medications used to achieve and maintain control of persistent asthma and quick-relief medications used to treat acute symptoms and exacerbations.

### **Long-Term Control Medications (Listed in Alphabetical Order)**

- **Corticosteroids:** Block late-phase reaction to allergen, reduce airway hyperresponsiveness, and inhibit inflammatory cell migration and activation. They are the most potent and effective anti-inflammatory medication currently available (**Evidence A**). Inhaled corticosteroids (ICSs) are used in the long-term control of asthma. Short courses of oral systemic corticosteroids are often used to gain prompt control of the disease when initiating long-term therapy; long-term oral systemic corticosteroid is used for severe persistent asthma.
- **Cromolyn sodium and nedocromil:** Stabilize mast cells and interfere with chloride channel function. They are used as alternative, but not preferred, medication for the treatment of mild persistent asthma (**Evidence A**). They can also be used as preventive treatment prior to exercise or unavoidable exposure to known allergens.
- **Immunomodulators:** Omalizumab (anti-immunoglobulin E [IgE]) is a monoclonal antibody that prevents binding of IgE to the high-affinity receptors on basophils and mast cells. Omalizumab is used as adjunctive therapy for patients  $\geq 12$  years of age who have allergies and severe persistent asthma (**Evidence B**). Clinicians who administer omalizumab should be prepared and equipped to identify and treat anaphylaxis that may occur (see discussion in the text of the original guideline document).
- **Leukotriene modifiers:** Include leukotriene receptor antagonists (LTRAs) and a 5-lipoxygenase inhibitor. Two LTRAs are available—montelukast (for patients  $> 1$  year of age) and zafirlukast (for patients  $\geq 7$  years of age). The 5-lipoxygenase pathway inhibitor zileuton is available for patients  $\geq 12$  years of age; liver function monitoring is essential. LTRAs are alternative, but not preferred, therapy for the treatment of mild persistent asthma (Step 2 care) (**Evidence A**). LTRAs can also be used as adjunctive therapy with ICSs, but for youths  $\geq 12$  years of age and adults they are not the preferred adjunctive therapy compared to the addition of long-acting beta<sub>2</sub>-agonist(s) (LABAs) (**Evidence A**). Zileuton can be used as alternative but not preferred adjunctive therapy in adults (**Evidence D**).

- **LABAs:** Salmeterol and formoterol are bronchodilators that have a duration of bronchodilation of at least 12 hours after a single dose.
  - LABAs are not to be used as monotherapy for long-term control of asthma (**Evidence A**).
  - LABAs are used in combination with ICSs for long-term control and prevention of symptoms in moderate or severe persistent asthma (step 3 care or higher in children  $\geq 5$  years of age and adults) (**Evidence A** for  $\geq 12$  years of age, **Evidence B** for 5 to 11 years of age)
  - Of the adjunctive therapies available, LABA is the preferred therapy to combine with ICS in youths  $\geq 12$  years of age and adults (**Evidence A**).
  - In the opinion of the Expert Panel, the beneficial effects of LABA in combination therapy for the great majority of patients who require more therapy than low-dose ICS alone to control asthma (i.e., require step 3 care or higher) should be weighed against the increased risk of severe exacerbations, although uncommon, associated with the daily use of LABAs (see discussion in the text of the original guideline document).
    - For patients  $\geq 5$  years of age who have moderate persistent asthma or asthma inadequately controlled on low-dose ICS, the option to increase the ICS dose should be given equal weight to the option of adding LABA.
    - For patients  $\geq 5$  years of age who have severe persistent asthma or asthma inadequately controlled on step 3 care, the combination of LABA and ICS is the preferred therapy.
  - LABA may be used before exercise to prevent exercise-induced bronchospasm (EIB) (**Evidence A**), but duration of action does not exceed 5 hours with chronic regular use. Frequent and chronic use of LABA for EIB is discouraged, because this use may disguise poorly controlled persistent asthma (**Evidence D**).
  - In the opinion of the Expert Panel, the use of LABA for the treatment of acute symptoms or exacerbations is not currently recommended (**Evidence D**).
- **Methylxanthines:** Sustained-release theophylline is a mild to moderate bronchodilator used as alternative, not preferred, adjunctive therapy with ICS (**Evidence A**). Theophylline may have mild anti-inflammatory effects. Monitoring of serum theophylline concentration is essential.

### Quick-Relief Medications (Listed in Alphabetical Order)

- **Anticholinergics:** Inhibit muscarinic cholinergic receptors and reduce intrinsic vagal tone of the airway. Ipratropium bromide provides additive benefit to short-acting beta<sub>2</sub>-agonist(s) (SABA) in moderate-to-severe asthma exacerbations. May be used as an alternative bronchodilator for patients who do not tolerate SABA (**Evidence D**).
- **SABAs:** Albuterol, levalbuterol, and pirbuterol are bronchodilators that relax smooth muscle. Therapy of choice for relief of acute symptoms and prevention of EIB (**Evidence A**).
- **Systemic corticosteroids:** Although not short acting, oral systemic corticosteroids are used for moderate and severe exacerbations as adjunct to

SABAs to speed recovery and prevent recurrence of exacerbations (**Evidence A**).

### **Key Differences from the 1997 and 2002 Expert Panel Reports**

- Information about asthma medications has been updated based on review of evidence published since 1997. *This updated report (EPR—3: Full Report 2007) continues to emphasize that the most effective medications for long-term therapy are those shown to have anti-inflammatory effects.*
- New medications—immunomodulators—are available for long-term control of asthma.
- New data on the safety of LABAs are discussed, and the position of LABA in therapy has been revised (see text in the original guideline document). The most significant difference is that for youths  $\geq 12$  years of age and adults who have moderate persistent asthma or asthma inadequately controlled on low-dose ICS, the option of increasing the dose of medium-dose ICS should be given equal weight to the option of adding LABA to low-dose ICS.
- The estimated clinical comparability of different ICS preparations has been updated. (See the NGC summaries of the NAEPP guidelines [Managing Asthma Long Term in Children 0-4 Years of Age and 5-11 Years of Age](#) and [Managing Asthma Long Term in Youths >12 Years of Age and Adults](#)). The significant role of ICSs in asthma therapy continues to be supported.

### **Overview of the Medications**

#### **Long Term Control Medications**

The Expert Panel recommends that long-term control medications be taken daily on a long-term basis to achieve and maintain control of persistent asthma. The most effective long-term-control medications are those that attenuate the underlying inflammation characteristic of asthma (**Evidence A**).

#### *Inhaled Corticosteroids*

##### Mechanism

The Expert Panel concludes that ICSs are the most potent and consistently effective long-term control medication for asthma (**Evidence A**).

##### Inhaled Corticosteroid Insensitivity

The Expert Panel concludes that sensitivity and consequently clinical response to ICS can vary among patients (**Evidence B**).

##### Efficacy of Inhaled Corticosteroids as Compared to Other Long-Term Control Medications as Monotherapy

The Expert Panel concludes that studies demonstrate that ICSs improve asthma control more effectively in both children and adults than LTRAs or any other single long-term control medication (**Evidence A**).

## Efficacy of Inhaled Corticosteroid and Adjunctive Therapy (Combination Therapy)

The Expert Panel recommends that when patients  $\geq 12$  years of age require more than low-dose ICS alone to control asthma (i.e., step 3 care or higher), a therapeutic option is to add LABA to ICS (**Evidence A**). Alternative, but not preferred adjunctive therapies include LTRA (**Evidence B**), theophylline (**Evidence B**), or, in adults, zileuton (**Evidence D**). For children 0–11 years of age, LABA, LTRA, and, in children 5–11 years of age, theophylline may be considered as adjunctive therapies in combination with ICS (**Evidence B**, based on extrapolation from studies in older children and adults; see also the NGC summaries of the NAEPP guidelines [Managing Asthma Long Term in Children 0-4 Years of Age and 5-11 Years of Age](#) and [Managing Asthma Long Term in Youths >12 Years of Age and Adults](#) for recommendations on adjunctive therapies at different steps of care for different age groups in children).

## Dose-Response and Delivery Device

The Expert Panel concludes that dosages for ICSs vary, depending upon the specific product and delivery devices. (See figure 3–24 in the original guideline document for issues on delivery devices; see the NGC summaries of the NAEPP guidelines [Managing Asthma Long Term in Children 0-4 Years of Age and 5-11 Years of Age](#) and [Managing Asthma Long Term in Youths >12 Years of Age and Adults](#) for comparative ICS dosages.) For all ICS preparations, the dose-response relationship appears to flatten in patients who have mild or moderate asthma for most clinical parameters and lung function in the low- to medium-dose range (**Evidence C**).

## Variability in Response and Adjustable Dose Therapy

The Expert Panel recommends that, given the variations over time in the severity of the pathophysiologic processes underlying asthma, it may be useful to adjust anti-inflammatory therapy accordingly (**Evidence B**).

## Safety of Inhaled Corticosteroids

### Key Points: Safety of Inhaled Corticosteroids

- ICSs are the most effective long-term therapy available for mild, moderate, or severe persistent asthma; in general, ICSs are well tolerated and safe at the recommended dosages (**Evidence A**).
- The potential but small risk of adverse events from the use of ICS treatment is well balanced by their efficacy (**Evidence A**).
- The dose-response curve for ICS treatment begins to flatten for many measures of efficacy at low to medium doses, although some data suggest that higher doses may reduce the risk of exacerbations. Most benefit is achieved with relatively low doses, whereas the risk of adverse effects increases with dose (**Evidence B**).
- To reduce the potential for adverse effects, the following measures are recommended:
  - Spacers or valved holding chambers (VHCs) used with non-breath-activated metered dose inhalers (MDIs) reduce local side effects

**(Evidence A)**, but there are no data on use of spacers with ultra fine particle hydrofluoroalkane (HFA) MDIs.

- Advise patients to rinse their mouths (rinse and spit) after inhalation **(Evidence B)**.
- Use the lowest dose of ICS that maintains asthma control. Evaluate patient adherence and inhaler technique as well as environmental factors that may contribute to asthma severity before increasing the dose of ICS **(Evidence B)**.
- To achieve or maintain control of asthma, consider adding a LABA to a low or medium dose of ICS rather than using a higher dose of ICS **(Evidence A)**.
- For children, monitor growth **(Evidence A)**. (See "Key Points: Inhaled Corticosteroids and Linear Growth in Children" below).
- In adult patients, consider supplements of calcium (1,000–1,500 mg per day) and vitamin D (400–800 units a day), particularly in perimenopausal women **(Evidence D)**. Bone-sparing therapy (e.g., bisphosphonate), where appropriate, may be considered for patients on medium or high doses of ICS, particularly for those who are at risk of osteoporosis or who have low bone mineral density (BMD) scores by dual energy x ray absorptiometry (or DEXA) scan **(Evidence C)**. In children, age-appropriate dietary intake of calcium and exercise should be reviewed with the child's caregivers **(Evidence D)**.

The Expert Panel concludes that ICSs are the most effective long-term therapy available for patients who have persistent asthma and, in general, ICSs are well tolerated and safe at the recommended dosages **(Evidence A)**.

The Expert Panel recommends the following actions to minimize potential adverse effects of ICS.

#### Local Adverse Effects

- Oral Candidiasis (Thrush). Use a spacer or VHC with a non-breath-activated MDI to reduce the incidence of colonization and clinical thrush; rinse mouth with water after inhalation (Selroos and Halme, 1991). No data are available on the use of spacers or VHCs with ultrafine-particle-generated HFA MDIs. Administer ICS less frequently (twice a day [bid] versus four times a day [qid]). Topical or oral antifungal agents should be used to treat active infections **(EPR–2 1997)**.
- Dysphonia. Use a spacer or VHC with a non-breath-activated MDI, temporarily reduce dosage, or rest for vocal stress **(EPR–2 1997)**.
- Reflex Cough And Bronchospasm. These effects can be reduced by slower rates of inspiration and/or use of a spacer or valved holding chamber or by pretreatment with SABA. There is no convincing evidence that the routine use of a SABA before each dose of ICS increases intrapulmonary delivery of the ICS or reduces dosage requirement **(EPR–2 1997)**.

#### Systemic Adverse Effects

- Linear Growth. Physicians should monitor the growth of children and adolescents who are taking corticosteroids by any route and should weigh the benefits of corticosteroid therapy and asthma control against the possibility of

growth suppression or delay if a child's or an adolescent's growth appears slowed (**Evidence D**).

#### Key Points: Inhaled Corticosteroids and Linear Growth in Children

In the opinion of the Expert Panel:

- The potential risks of ICSs are well balanced by their benefits.
- Growth rates are highly variable in children. Short-term evaluations may not be predictive of final adult height attained.
- Poorly controlled asthma may delay growth in children.
- In general, children who have asthma tend to have longer periods of reduced growth rates before puberty (males more than females).
- The potential for adverse effects on linear growth from ICS appears to be dose dependent. In treatment of children who have *mild or moderate persistent asthma*, low- to medium-dose ICS therapy may be associated with a possible, but not predictable, adverse effect on linear growth. The clinical significance of this potential systemic effect has yet to be determined. High doses of ICS have greater potential for growth suppression.
- Use of high doses of ICS by children who have *severe persistent asthma* has significantly less potential than use of oral systemic corticosteroids for having an adverse effect on linear growth.
- Studies in which growth has been carefully monitored suggest the growth-velocity effect of ICS occurs in the first several months of treatment and is generally small and nonprogressive.
- In general, the efficacy of ICSs is sufficient to outweigh any concerns about growth or other systemic effects. However, ICSs, as with any medications, should be titrated to as low a dose as needed to maintain good control of the child's asthma.
- Bone Mineral Density. In patients who have risk factors for osteoporosis or low BMD scores, consideration can be given to bone-protecting therapies (e.g., bisphosphonates), although data are mixed in supporting the use of these therapies specifically in asthma patients who are taking ICS (Campbell et al., 2004; Kasayama et al., 2005) (**Evidence C**). Measuring BMD may be considered every 1–2 years, depending on duration and dose of ICS and oral corticosteroid treatment as well as previous BMD scores (**Evidence D**).
- Disseminated Varicella. Children who require episodic therapy with systemic corticosteroids and who have not had clinical varicella should receive the varicella vaccine (**EPR—2 1997**). The vaccine should not be administered to patients who are receiving immunosuppressive doses of systemic corticosteroids (2 mg/kg or more of prednisone equivalent or 20 mg/day of prednisone for more than 1 month), unless this dosage is discontinued for at least 1 month. Children who have completed a short prednisone course may receive varicella vaccine without delay ("Recommendations," 1995; Advisory Committee on Immunization Practices, 1994). Children and adults on treatment with immunosuppressive doses of corticosteroids who have not been immunized against varicella and are exposed to varicella infection are candidates for oral antiviral therapy (e.g., valacyclovir). If they develop clinical varicella, intravenous antiviral therapy should be given (**EPR—2 1997**).

- Ocular Effects. Data suggest the advisability of periodic assessments and treatments, if indicated, for increased intraocular pressures in asthma patients who use ICS, particularly at higher doses, and have a family history of glaucoma (**Evidence C**).

#### *Oral Systemic Corticosteroids*

The Expert Panel recommends that chronic administration of oral systemic corticosteroids as a long-term-control medication be used only for the most severe, difficult-to-control asthma because of well-documented risk for side effects (**EPR—2 1997**).

The Expert Panel recommends that, because the magnitude of adverse effects is often related to the dose, frequency of administration, and the duration of corticosteroid use (**Evidence A**), every consideration should be given to minimize systemic corticosteroid doses and maximize other modes of therapy (**Evidence D**). It is necessary, therefore, to monitor for the development and progression of adverse effects and to take appropriate steps to minimize the risk and impact of adverse corticosteroid effects (**Evidence D**).

#### *Cromolyn Sodium and Nedocromil*

Cromolyn and nedocromil are alternative, not preferred, medications for the treatment of mild persistent asthma (**Evidence A**). They can also be used as preventive treatment before exercise or unavoidable exposure to known allergens (**EPR—2 1997**).

#### *Immunomodulators*

##### Omalizumab

The Expert Panel recommends that omalizumab may be considered as adjunctive therapy in step 5 or 6 care for patients who have allergies and severe persistent asthma that is inadequately controlled with the combination of high-dose ICS and LABA (**Evidence B**).

##### Antibiotics

In the opinion of the Expert Panel, the data at present are insufficient to support a recommendation about the use of macrolide in chronic asthma.

##### Others

The Expert Panel concludes that current evidence does not support the use of methotrexate, soluble interleukin-4 (IL-4) receptor, humanized monoclonal antibody against IL-5 or IL-12, cyclosporin A, intravenous immunoglobulin (IVIG), gold, troleandomycin (TAO), or colchicine for asthma treatment (**Evidence B**).

#### *Leukotriene Modifiers*

The Expert Panel recommends that LTRAs are an alternative, not preferred, treatment option for mild persistent asthma (Step 2 care) (**Evidence A**). LTRAs can also be used as adjunct therapy with ICS, but for youths  $\geq 12$  years of age and adults they are not the preferred, adjunct therapy compared to the addition of LABAs (**Evidence A**). A 5-lipoxygenase inhibitor (zileuton) is an alternative treatment option that is less desirable than LTRAs due to more limited efficacy data and the need for liver function monitoring (**Evidence D**).

### *Inhaled Long-Acting Beta<sub>2</sub>-Agonists*

The Expert Panel concludes the following regarding the use of LABAs:

- LABAs are used as an adjunct to ICS therapy for providing long-term control of symptoms (**Evidence A**). Of the adjunctive therapies available, LABA is the preferred treatment to combine with ICS in youths  $\geq 12$  years of age and adults (**Evidence A**).
- LABAs are not recommended for use as monotherapy for long-term control of persistent asthma (**Evidence A**).
- Use of LABA is not currently recommended to treat acute symptoms or exacerbations of asthma (**Evidence D**). Studies are underway examining the potential use of formoterol in acute exacerbations and in adjustable-dose therapy in combination with ICS; see the discussion below in the section on "Quick-Relief Medications" and on "Inhaled Short-Acting Beta<sub>2</sub>-Agonists."
- LABA may be used before exercise to prevent EIB (**Evidence B**), but frequent and chronic use of LABA for EIB may indicate poorly controlled asthma which should be managed with daily anti-inflammatory therapy.
- Safety issues have been raised regarding LABAs. The Expert Panel reviewed the safety data provided to the U.S. Food and Drug Administration (FDA) Pulmonary and Allergy Drugs Advisory Committee as well as the extensive accumulation of clinical trials and meta-analyses on the use of LABA, both as monotherapy and in conjunction with ICS. The Expert Panel concluded that LABAs should not be used as monotherapy as long-term control medication in persistent asthma but that LABAs should continue to be considered for adjunctive therapy in patients  $\geq 5$  years of age who have asthma that requires more than low-dose ICS. For patients inadequately controlled on low-dose ICS, the option to increase the ICS dose should be given equal weight to the addition of a LABA. For patients who have more severe persistent asthma (i.e., those who require step 4 care or higher), the Expert Panel continues to endorse the use of a combination of LABA and ICS as the most effective therapy. The basis of this opinion is discussed in the original guideline document.

### Key Points: Safety of Inhaled Long-Acting Beta<sub>2</sub>-Agonists

- The addition of LABA (salmeterol or formoterol) to the treatment of patients whose asthma is not well controlled on low- or medium-dose ICS improves lung function, decreases symptoms, and reduces exacerbations and use of SABA for quick relief in most patients (**EPR-Update 2002**; Greenstone et al., 2005; Masoli et al., 2005).
- A large clinical trial comparing daily treatment with salmeterol or placebo added to usual asthma therapy (Nelson et al., 2006) resulted in an increased risk of asthma-related deaths in patients treated with salmeterol (13 deaths

out of 13,176 patients treated for 28 weeks with salmeterol versus 3 deaths out of 13,179 patients with placebo). In addition, increased numbers of severe asthma exacerbations were noted in the pivotal trials submitted to the FDA for formoterol approval, particularly in the higher dose formoterol arms of the trials (Mann et al., 2003). Thus the FDA determined that a Black Box warning was warranted on all preparations containing a LABA.

- The Expert Panel recommends that the established, beneficial effects of LABA for the great majority of patients whose asthma is not well controlled with ICS alone should be weighed against the increased risk for severe exacerbations, although uncommon, associated with the daily use of LABAs.
- Therefore, the Expert Panel has modified its previous recommendation (EPR—Update 2002) and has now concluded that, for patients who have asthma not sufficiently controlled with ICS alone, the option to increase the ICS dose should be given equal weight to the option of the addition of a LABA to ICS.
- Daily use of LABA generally should not exceed 100 micrograms salmeterol or 24 micrograms formoterol.
- It is not currently recommended that LABA be used for treatment of acute symptoms or exacerbations.
- LABAs are not to be used as monotherapy for long-term control. Patients should be instructed not to stop ICS therapy while taking salmeterol or formoterol even though their symptoms may significantly improve.

#### *Methylxanthines*

The Expert Panel recommends that sustained-release theophylline is an alternative but not preferred treatment for mild persistent asthma (Step 2 care) **(Evidence A)**; it may also be used as alternative but not preferred adjunctive therapy with ICS **(Evidence B)**.

### **Quick Relief Medications**

#### *Anticholinergics*

The Expert Panel concludes that ipratropium bromide, administered in multiple doses along with SABA in moderate or severe asthma exacerbations in the ED, provides additive benefit **(Evidence B)**.

#### *Inhaled Short-Acting Beta<sub>2</sub>-Agonists*

The Expert Panel recommends that SABAs are the drug of choice for treating acute asthma symptoms and exacerbations and for preventing EIB **(Evidence A)**.

#### Safety of Inhaled Short-Acting Beta<sub>2</sub>-Agonists

##### Key Points: Safety of Inhaled Short-Acting Beta<sub>2</sub>-Agonists

- SABAs are the most effective medication for relieving acute bronchospasm **(Evidence A)**.
- Increasing use of SABA treatment or using SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control

of asthma and the need for initiating or intensifying anti-inflammatory therapy **(Evidence C)**.

- Regularly scheduled, daily, chronic use of SABA is not recommended **(Evidence A)**.

The Expert Panel recommends the use of SABA as the most effective medication for relieving acute bronchoconstriction; SABAs have few negative cardiovascular effects **(Evidence A)**.

The Expert Panel does not recommend regularly scheduled, daily, long-term use of SABA **(Evidence A)**.

### *Systemic Corticosteroids*

The Expert Panel recommends the use of oral systemic corticosteroids in moderate or severe exacerbations **(Evidence A)**.

The Expert Panel recommends that multiple courses of oral systemic corticosteroids, especially more than three courses per year, should prompt a reevaluation of the asthma management plan for a patient **(Evidence C)**.

## **Complementary and Alternative Medicine**

### **Key Points: Complementary and Alternative Medicine**

- It is recommended that the clinician ask patients about all medications and treatments they are using for asthma and advise the patients that complementary and alternative medicines and treatments are not a substitute for the clinician's recommendations for asthma treatment **(Evidence D)**.
- Evidence is insufficient to recommend or not recommend most complementary and alternative medicines or treatments.
- Acupuncture is not recommended for the treatment of asthma **(Evidence B)**.
- Patients who use herbal treatments for asthma should be cautioned that there is the potential for harmful ingredients in herbal treatments and for interactions with recommended asthma medications **(Evidence D)**

### **Acupuncture**

The Expert Panel does not recommend the use of acupuncture for the treatment of asthma **(Evidence B)**.

### **Chiropractic Therapy**

The Expert Panel concludes that there is insufficient evidence to recommend the use of chiropractic or related techniques in the treatment of asthma.

### **Homeopathy and Herbal Medicine**

The Expert Panel concludes that there is insufficient evidence to support effectiveness of homeopathy and that more clinical trial and observational data are necessary.

The Expert Panel concludes that there is insufficient evidence to recommend herbal products for treating asthma. Furthermore, because herbal products are not standardized, one must be aware that some may have harmful ingredients and that some may interact with other pharmaceutical products that the patient may be taking (**Evidence D**).

### **Breathing Techniques**

The Expert Panel concludes there is insufficient evidence to suggest that breathing techniques provide clinical benefit to patients who have asthma.

### **Relaxation Techniques**

The Expert Panel concludes that, despite some encouraging data from small studies, further positive data from randomized, controlled studies will be necessary before relaxation techniques can be recommended in the treatment of asthma.

### **Yoga**

There is a paucity of well-controlled studies on the effects of yoga on asthma outcomes.

### **Definitions:**

#### **Levels of Evidence**

The system\* used to describe the level of evidence is as follows:

#### **Evidence Category A: Randomized controlled trials (RCTs), rich body of data.**

Evidence is from end points of well-designed RCTs that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.

#### **Evidence Category B: RCTs, limited body of data.**

Evidence is from end points of intervention studies that include only a limited number of patients, post hoc or subgroup analysis of RCTs, or meta-analysis of RCTs. In general, category B pertains when few randomized trials exist; they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.

#### **Evidence Category C: Nonrandomized trials and observational studies.**

Evidence is from outcomes of uncontrolled or nonrandomized trials or from observational studies.

#### **Evidence Category D: Panel consensus judgment.**

This category is used only in cases where the provision of some guidance was deemed valuable, but the clinical literature addressing the subject was insufficient to justify placement in one of the other categories. The Panel consensus is based

on clinical experience or knowledge that does not meet the criteria for categories A through C.

\*Source: Jadad AR, Moher M, Browman GP, Booker L, Sigouin C, Fuentes M, Stevens R. Systematic reviews and meta-analyses on treatment of asthma: critical evaluation. *BMJ* 2000;320(7234):537-40.

### **Strength of Recommendations**

In addition to specifying the level of evidence supporting a recommendation, the Expert Panel agreed to indicate the strength of the recommendation. When a certain clinical practice "is recommended," this indicates a strong recommendation by the panel. When a certain clinical practice "should, or may, be considered," this indicates that the recommendation is less strong.

This distinction is an effort to address nuances of using evidence ranking systems. For example, a recommendation for which clinical RCT data are not available (e.g., conducting a medical history for symptoms suggestive of asthma) may still be strongly supported by the Panel. Furthermore, the range of evidence that qualifies a definition of "B" or "C" is wide, and the Expert Panel considered this range and the potential implications of a recommendation as they decided how strongly the recommendation should be presented.

### **CLINICAL ALGORITHM(S)**

None provided

## **EVIDENCE SUPPORTING THE RECOMMENDATIONS**

### **REFERENCES SUPPORTING THE RECOMMENDATIONS**

[References open in a new window](#)

### **TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS**

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

## **BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS**

### **POTENTIAL BENEFITS**

- Prevention and control of asthma symptoms
- Improved quality of life
- Reduction in the frequency and severity of asthma exacerbations
- Reversal of airflow obstruction

### **POTENTIAL HARMS**

Potential adverse effects of long-term control and quick-relief medications are listed in figures 3-22 and 3-23 of the original guideline document. See also the "Major Recommendations" section of this summary for "safety key points" related to inhaled corticosteroids and inhaled long-acting and short-acting beta<sub>2</sub>-agonists.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

These guidelines are intended to inform, not replace, clinical judgment. Of course, the clinician and patient need to develop individual treatment plans that are tailored to the specific needs and circumstances of the patient.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

### IMPLEMENTATION TOOLS

Foreign Language Translations  
Patient Resources  
Quick Reference Guides/Physician Guides  
Resources

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Living with Illness  
Staying Healthy

### IOM DOMAIN

Effectiveness  
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Medications. In: National Asthma Education and Prevention Program (NAEPP). Expert panel report 3: guidelines for the diagnosis and management of asthma.

Bethesda (MD): National Heart, Lung, and Blood Institute; 2007 Aug. p. 213-76.  
[315 references]

#### **ADAPTATION**

Not applicable: The guideline was not adapted from another source.

#### **DATE RELEASED**

1997 (revised 2007 Aug)

#### **GUIDELINE DEVELOPER(S)**

National Asthma Education and Prevention Program - Federal Government Agency  
[U.S.]  
National Heart, Lung, and Blood Institute (U.S.) - Federal Government Agency  
[U.S.]

#### **GUIDELINE DEVELOPER COMMENT**

The National Asthma Education and Prevention Program Science Base Committee is a multidisciplinary group of clinicians and scientists with expertise in asthma management. The group includes health professionals in the areas of general medicine, family practice, pediatrics, emergency and critical care, allergy, pulmonary medicine, pharmacy, and health education.

#### **SOURCE(S) OF FUNDING**

The development of this report was entirely funded by the National Heart, Lung, and Blood Institute, National Institutes of Health.

#### **GUIDELINE COMMITTEE**

National Asthma Education and Prevention Program (NAEPP) Coordinating  
Committee  
Third Expert Panel on the Diagnosis and Management of Asthma

#### **COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE**

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See the original guideline document for members of the National Asthma Education and Prevention Program (NAEPP) Coordinating Committee, a list of consultant reviewers, and members of the National Heart, Lung, and Blood Institute and American Institutes for Research staffs.

## **FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST**

Development of the resource document and the guidelines report was funded by the National Heart, Lung, and Blood Institute (NHLBI), and National Institutes of Health (NIH). Expert Panel members completed financial disclosure forms, and the Expert Panel members disclosed relevant financial interests to each other prior to their discussions. Expert Panel members participated as volunteers and were compensated only for travel expenses related to the Expert Panel meetings. Financial disclosure information covering the 3-year period during which the guidelines were developed is provided for each Panel member below.

Dr. Busse has served on the Speakers' Bureaus of GlaxoSmithKline, Merck, Novartis, and Pfizer; and on the Advisory Boards of Altana, Centocor, Dynavax, Genentech/Novartis, GlaxoSmithKline, Isis, Merck, Pfizer, Schering, and Wyeth. He has received funding/grant support for research projects from Astellas, AstraZeneca, Centocor, Dynavax, GlaxoSmithKline, Novartis, and Wyeth. Dr. Busse also has research support from the NIH.

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Dr. Evans has received funding/grant support for research projects from the NHLBI.

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as consultant for Merck and Sepracor. He has received funding/grant support for research projects from GlaxoSmithKline.

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Dr. Platts-Mills has served on the Advisory Committee of Indoor Biotechnologies. He has received funding/grant support for a research project from Pharmacia Diagnostics.

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Dr. Shapiro (deceased) served on the Speakers' Bureaus of AstraZeneca, Genentech, GlaxoSmithKline, IVAX Laboratories, Key Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Schering Corporation, UCB Pharma, and 3M; and as a consultant for Altana, AstraZeneca, Dey Laboratories, Genentech/Novartis, GlaxoSmithKline, ICOS, IVAX Laboratories, Merck, Sanofi-Aventis, and Sepracor. She received funding/grant support for research projects from Abbott, AstraZeneca, Boehringer Ingelheim, Bristol-Myers-Squibb, Dey Laboratories, Fujisawa Pharmaceuticals, Genentech, GlaxoSmithKline, Immunex, Key, Lederle, Lilly Research, MedPointe Pharmaceuticals, Medtronic Emergency Response

Systems, Merck, Novartis, Pfizer, Pharmaxis, Purdue Frederick, Sanofi-Aventis, Schering, Sepracor, 3M Pharmaceuticals, UCB Pharma, and Upjohn Laboratories.

Dr. Stoloff has served on the Speakers' Bureaus of Alcon, Altana, AstraZeneca, Genentech, GlaxoSmithKline, Novartis, Pfizer, Sanofi-Aventis, and Schering; and as a consultant for Alcon, Altana, AstraZeneca, Dey, Genentech, GlaxoSmithKline, Merck, Novartis, Pfizer, Sanofi-Aventis, and Schering.

Dr. Szeffler has served on the Advisory Boards of Altana, AstraZeneca, Genentech, GlaxoSmithKline, Merck, Novartis, and Sanofi-Aventis; and as a consultant for Altana, AstraZeneca, Genentech, GlaxoSmithKline, Merck, Novartis, and Sanofi-Aventis. He has received funding/grant support for a research project from Ross.

Dr. Weiss has served on the Advisory Board of Genentech, and as a consultant for Genentech and GlaxoSmithKline. He has received funding/grant support for research projects from GlaxoSmithKline.

Dr. Yawn has served on the Advisory Boards of Altana, AstraZeneca, Merck, Sanofi-Aventis, and Schering-Plough. She has received honoraria from Pfizer and Schering-Plough, and funding/grant support for research projects from the Agency for Healthcare Research and Quality, the CDC, the NHLBI, Merck, and Schering-Plough.

Financial disclosure information covering a 12 month period prior to the review of the guidelines is provided in the original guideline document for each consultant reviewer.

## **GUIDELINE STATUS**

This is the current release of the guideline.

This guideline updates a previous version: National Asthma Education and Prevention Program Expert Panel Report: guidelines for the diagnosis and management of asthma update on selected topics-2002. *J Allergy Clin Immunol* 2002 Nov;110(5 pt 2):S141-219.

## **GUIDELINE AVAILABILITY**

Electronic copies: Available from the [National Heart, Lung, and Blood Institute Web site](#).

Print copies: Available from NHLBI Information Center, P.O. Box 30105, Bethesda, MD 20824-0105; e-mail: [nhlbiic@dgsys.com](mailto:nhlbiic@dgsys.com).

## **AVAILABILITY OF COMPANION DOCUMENTS**

The following are available:

- Guidelines for the diagnosis and management of asthma. Summary report 2007. Bethesda (MD): National Heart, Lung, and Blood Institute; 2007. Available from the [National Heart, Lung, and Blood Institute Web site](#).

- Overall methods used to develop this report. Electronic copies: Available from the [National Heart, Lung, and Blood Institute Web site](#).
- Search strategies. Electronic copies: Available from the [National Heart, Lung, and Blood Institute Web site](#).
- Evidence tables. Electronic copies: Available from the [National Heart, Lung, and Blood Institute Web site](#).
- Lung diseases information. Information for health professionals. Electronic copies: Available from the [National Heart, Lung, and Blood Institute Web site](#).

Print copies: Available from NHLBI Information Center, P.O. Box 30105, Bethesda, MD 20824-0105; e-mail: [nhlbic@dgsys.com](mailto:nhlbic@dgsys.com).

## **PATIENT RESOURCES**

The following is available:

- Lung diseases information. Information for patients and the public.

Electronic copies: Available from the [National Heart, Lung and Blood Institute Web site](#).

Print copies: Available from NHLBI Information Center, P.O. Box 30105, Bethesda, MD 20824-0105; e-mail: [nhlbic@dgsys.com](mailto:nhlbic@dgsys.com).

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## **NGC STATUS**

This summary was completed by ECRI on January 5, 1999. The information was verified by the guideline developer on April 30, 1999. This summary was updated by ECRI on January 31, 2003. This information was not verified by the guideline developer. This summary was updated by ECRI on December 5, 2005 following the U.S. Food and Drug Administration (FDA) advisory on long-acting beta2-adrenergic agonists (LABA). This NGC summary was updated by ECRI Institute on January 14, 2008.

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