

## Stepwise Approach for Managing Asthma<sup>1</sup>

### CareFirst BlueCross BlueShield (CareFirst) and CareFirst BlueChoice, Inc. (CareFirst BlueChoice) Preferred Drug List Choices for Managing Children and Adults with Asthma (2007):

#### β<sub>2</sub>-agonists

- Albuterol (Tier 1)
- Albuterol SR  
maintenance use only (Tier 1)
- Ventolin HFA  
maintenance use only (Tier 2)
- Albuterol (VENTOLIN®) (Tier 3)
- Metaproterenol (Tier 1)
- Metaproterenol inhaler (ALUPENT®) (Tier 3)
- Salmeterol (SEREVENT®)  
maintenance use only (Tier 2)
- Pirbuterol (MAXAIR AUTOHALER®) (Tier 3)

#### Methylxanthines

- Theophylline (Tier 1)
- THEO-DUR®, THEO-X® (Tier 2)

#### Miscellaneous agents

- Montelukast (SINGULAIR®)\* (Tier 2)
- Zafirlukast (ACCOLATE®)\*\*  
maintenance use only (Tier 2)

#### Miscellaneous inhalers

- Cromolyn sodium (Tier 1)
- Cromolyn sodium (INTAL®) (Tier 3)
- Ipratropium bromide inhaler  
maintenance use only (Tier 1)
- Ipratropium bromide inhaler (COMBIVENT®) (Tier 2)
- Ipratropium inhaler (ATROVENT®) (Tier 2)
- Formoterol inhaler (FORADIL®) (Tier 2)
- Nedocromil sodium (TILADE®) (Tier 2)
- Flunisolide inhaler (AEROBID®) (Tier 3)

- Levabuterol inhaler (XOPENEX®) (Tier 3)
- Tiotropium bromide inhalation powder (SPIRIVA®) maintenance use only (Tier 2)

#### Inhaled steroids

- Beclomethasone (Tier 1)
- Beclomethasone (BECLOVENT®) (Tier 3)
- Budesonide (PULMICORT®) (Tier 2)
- Fluticasone (FLOVENT®) (Tier 2)
- Fluticasone+salmeterol inhaler (ADVAIR DISKUS®) (Tier 2)
- Triamcinolone (AZMACORT®) (Tier 2)

#### Oral steroids

- Prednisone (Tier 1)
- Prednisolone sodium (Tier 1)
- Prednisolone sodium (PRELONE®) (Tier 3)
- Dexamethasone (Tier 1)
- Dexamethasone (DECADRON®) (Tier 3)

#### Injectable Anti-IGE

- Omalizumab (XOLAIR®)  
prior authorization required (Tier 2)

CareFirst and CareFirst BlueChoice Preferred Drug List. Tier 1 generic drugs offer the lowest member copay, Tier 2 preferred brand name drugs are a higher member copay, Tier 3 non-preferred brand name drugs are the highest member copay.

For current information on the CareFirst and CareFirst BlueChoice Formulary and Tier designation, refer to the *Providers and Physicians* section of [www.carefirst.com](http://www.carefirst.com), click on *Prescription Drugs*, then *FAQs*.

\*Recommended for prophylaxis and chronic treatment of asthma in adults and children >2 years of age (Source: Adapted from Drug Acts and Comparisons, June 2000)

\*\*Recommended for prophylaxis and chronic treatment of asthma in pediatric patients 5-6 years of age (Source: Adapted from [www.accessdata.fda.gov/scripts/cder/drugsatfda](http://www.accessdata.fda.gov/scripts/cder/drugsatfda), 4/27/01)

## General Information

The stepwise approach presents general guidelines to assist clinical decision making. It is not intended to be a specific prescription. Asthma is highly variable; clinicians should tailor specific medication plans to the needs and circumstances of individual patients.

Gain control as quickly as possible, then decrease treatment to the least medication necessary to maintain control. Gaining control may be accomplished by either starting treatment at the step most appropriate to the initial severity of the condition or by starting at a higher level of therapy (e.g., a course of systemic corticosteroids or a higher dose of inhaled corticosteroids).

A rescue course of systemic corticosteroid (prednisolone) may be needed at any time and step. In general, use of short acting  $\beta$ 2-agonist on a daily basis indicates the need for additional long term control therapy. It is important to remember that there are very few studies on asthma therapy for infants.

<sup>1</sup>Adapted From: National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program. Expert Panel Report: *Guidelines for the Diagnosis and Management of Asthma - Update on Selected Topics 2002*. National Institutes of Health pub no 102-5074. Bethesda, MD. 2003.

Consultation with an asthma specialist is recommended for patients with moderate or severe persistent asthma in the age group, 5 years and younger. Consultation should be considered for all patients with mild persistent asthma.

**Severity of asthma**—Asthma can be classified by severity into four categories: severe persistent; moderate persistent; mild persistent and mild intermittent depending on the level and variability of airway obstruction.

### Long-term management of asthma—The aim of treatment is control of asthma

|   |  |
|---|--|
| Minimal (ideally no) chronic symptoms, including nocturnal symptoms | No limitations on activities, including exercise |
| Minimal (infrequent) episodes                                       | PEF circadian variation <20%                     |
| No emergency visits   | (Near) normal PEF                                |
| Minimal need for prn $\beta$ 2-agonists                             | Minimal (or no) adverse effects from medicine    |

## Major Recommendations from the Expert Panel Report 2: *Guidelines for the Diagnosis and Management of Asthma*<sup>2</sup>

### Diagnose asthma and initiate partnership with patient

- Diagnose asthma by establishing:
  - A history of recurrent symptoms.
  - Reversible airflow obstruction using spirometry.
  - The exclusion of alternative diagnoses.
- Establish patient-clinician partnership:
  - Address patient's concerns.
  - Agree upon the goals of asthma therapy.
  - Agree upon a written action plan for patient self-management.

<sup>2</sup>Practical Guide for the Diagnosis and Management of Asthma: National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program. Expert Panel Report 2: *Guidelines for the Diagnosis and Management of Asthma*. National Institutes of Health pub no 97-4051. Bethesda, MD. 1997.p.3.

## Reduce inflammation, symptoms and exacerbations

- Prescribe anti-inflammatory medications to patients with mild, moderate or severe persistent asthma (i.e., inhaled steroids, cromolyn or nedocromil).
- Reduce exposures to precipitants of asthma symptoms:
  - Assess patient's exposure and sensitivity to individual precipitants (e.g., allergens, irritants).
  - Provide written and verbal instructions on how to avoid or reduce factors that make the patient's asthma worse.

## Monitor and manage asthma over time

- Train all patients to monitor their asthma:
  - All patients should monitor symptoms.
  - Patients with moderate to severe persistent asthma should also monitor their peak flow.
- See patients at least every 1 to 6 months:
  - Assess attainment of goals of asthma therapy and patient's concerns.
  - Adjust treatment, if needed.
  - Review the action plan with patient.
  - Check patient's inhaler and peak flow technique.
  - Review environmental control.

## Treat asthma episodes promptly

- Prompt use of short acting inhaled  $\beta_2$ -agonists and if episode is moderate to severe, a 3 to 10-day course of oral steroids.
- Prompt communication and follow-up with clinician.

## Key Recommendations for Managing Asthma in Infants and Young Children

Diagnosing asthma in infants is often difficult, yet underdiagnosis and undertreatment are key problems in this age group. Thus, a diagnostic trial of inhaled bronchodilators and anti-inflammatory medications may be helpful.

Diagnosis is complicated by the difficulty in obtaining objective measurement of lung function in this age group. Essential elements in the evaluation include the history, symptoms, physical examination and assessment of quality of life.

The initiation of long-term control therapy should be considered in infants and young children who have had more than 3 episodes of wheezing in the past year that lasted more than 1 day and affected sleep and who have risk factors for the development of asthma (parental history of asthma or physician-diagnosed atopic dermatitis or 2 of the following: physician-diagnosed allergic rhinitis, wheezing apart from colds,  $>4\%$  peripheral blood eosinophilia).

In general, infants and young children consistently requiring symptomatic treatment more than two times per week or experiencing severe exacerbations (requiring inhaled  $\beta_2$ -agonist more frequently than every 4 hours over 24 hours) that occur less than 6 weeks apart should be given daily anti-inflammatory therapy.

Initiate daily anti-inflammatory therapy with inhaled corticosteroids.

Response to therapy should be carefully monitored. If there is no clear response within 4 to 6 weeks, therapy should be discontinued and alternative therapies or alternative diagnoses considered. If there is a clear and positive response after 2 to 4 months, a step down in therapy should be undertaken to the lowest possible doses of medication required to maintain asthma control.

# Pharmacology Therapy: Stepwise Approach for Managing Infants and Young Children

(5 years of age and younger) With Acute or Chronic Asthma Symptoms

|  | Long-Term Control   | Quick Relief  |
|--|---|---|
| <b>Step 1 Mild Intermittent</b>  |   |   |
| <ul style="list-style-type: none"> <li>■ Symptoms ≤ 2 times per week</li> <li>■ Brief exacerbations (from a few hours to a few days)</li> <li>■ Night time asthma symptoms ≤ 2 times per month</li> <li>■ Asymptomatic and normal lung function between exacerbations</li> </ul> | <p>No daily medication needed.</p>  | <p>Bronchodilator as needed for symptoms ≤ 2 times a week. Intensity of treatment will depend upon severity of exacerbation.</p> <p>Use of short-acting β<sub>2</sub>-agonists &gt;2 times a week may indicate the need to initiate long-term-control therapy.</p> <p>Either:</p> <ul style="list-style-type: none"> <li>■ Inhaled short acting β<sub>2</sub>-agonist by nebulizer or face mask and spacer/ holding chamber OR</li> <li>■ Oral β<sub>2</sub>-agonist for symptoms</li> </ul> <p><b>With viral respiratory infection:</b></p> <ul style="list-style-type: none"> <li>■ Bronchodilator q 4-6 hours up to 24 hours (longer with physician consult) but in general, repeat no more than once every 6 weeks.</li> </ul> <p>Consider systemic corticosteroid if current exacerbation is severe OR patient has history of previous severe exacerbations.</p> |
| <b>Step 2 Mild Persistent</b>  |   |   |
| <ul style="list-style-type: none"> <li>■ Symptoms &gt;2 times per week but &lt; 1 time per day</li> <li>■ Exacerbations may affect activity</li> <li>■ Night time asthma symptoms &gt; 2 times per month</li> </ul>  | <p><b>Preferred treatment:</b> Low dose inhaled corticosteroids with nebulizer or MDI.</p> <p><b>Alternative treatment:</b> Leukotriene receptor antagonist [i.e., Zafirlukast (Accolate®) or Montelukast (Singulair®) or Cromolyn (nebulizer preferred)].</p>  | <p>Bronchodilator as needed for symptoms (see Step 1).</p> <p>Increasing use of short-acting β<sub>2</sub>-agonists in persistent asthma may indicate the need to increase long-term-control therapy.</p>   |
| <b>Step 3 Moderate Persistent</b>  |   |   |
| <ul style="list-style-type: none"> <li>■ Symptoms daily</li> <li>■ Exacerbations ≥ 2 times per week; may last days</li> <li>■ Night time asthma symptoms &gt; 1 time per week</li> <li>■ Daily use of inhaled short acting β<sub>2</sub>-agonist</li> </ul>                      | <p><b>Preferred treatment:</b> Low dose inhaled corticosteroids AND long acting inhaled β<sub>2</sub>-agonists or medium dose inhaled corticosteroids.</p> <p><b>Alternative treatment:</b> Low dose inhaled corticosteroids and either long acting bronchodilator (i.e., Theophylline) or leukotriene receptor antagonist [i.e., Zafirlukast (Accolate®) or Montelukast (Singulair®)].</p> <p>If needed (particularly in patients with recurring severe exacerbations):</p> <ul style="list-style-type: none"> <li>■ Preferred treatment: medium-dose inhaled corticosteroids and long-acting β<sub>2</sub>-agonists</li> <li>■ Alternative treatment: medium-dose inhaled corticosteroids and either leukotriene receptor antagonist or theophylline</li> </ul> | <p>Bronchodilator as needed for symptoms (see Step 1) up to 3 times a day.</p> <p>Increasing use of short-acting β<sub>2</sub>-agonists in persistent asthma may indicate the need to increase long-term-control therapy.</p>   |
| <b>Step 4 Severe Persistent</b>  |   |   |
| <ul style="list-style-type: none"> <li>■ Continual symptoms</li> <li>■ Frequent exacerbations</li> <li>■ Frequent night time asthma symptoms</li> <li>■ Physical activities limited by asthma symptoms</li> </ul>  | <p><b>Preferred treatment:</b> High dose inhaled corticosteroids AND long acting inhaled β<sub>2</sub>-agonists AND if needed, oral corticosteroids (2 mg/kg/day, do not exceed 60mg/day).</p> <p>Make repeat attempts to reduce systemic corticosteroids and maintain control with high-dose inhaled corticosteroids.</p>  | <p>Bronchodilator as needed for symptoms (see Step 1) up to 3 times a day.</p> <p>Increasing use of short-acting β<sub>2</sub>-agonists in persistent asthma may indicate the need to increase long-term-control therapy.</p>   |

- ✓ Avoid or control triggers
- ✓ Patients should start treatment at the step most appropriate to the initial severity of their condition
- ✓ A rescue course of systemic corticosteroids may be needed at any time and at any step

# Stepwise Approach for Adults and Children

(older than 5 years of age) With Acute or Chronic Asthma Symptoms

|   | Long-Term Control  | Quick Relief  |
|---|--|---|
| <b>Step 1 Mild Intermittent</b>   |  |   |
| <ul style="list-style-type: none"> <li>■ Symptoms ≤ 2 times per week</li> <li>■ Brief exacerbations (from a few hours to a few days)</li> <li>■ Night time asthma symptoms ≤ 2 times per month</li> <li>■ Asymptomatic and normal lung function between exacerbations</li> <li>■ PEF or FEV<sub>1</sub> ≥ 80% predicted; PEF –variability &lt; 20%</li> </ul> | <p>No daily medication needed.</p> <p>If severe exacerbations occur followed by long periods of normal lung function and no symptoms, the recommendation is a course of systemic corticosteroids.</p>  | <p>Short acting inhaled β<sub>2</sub>-agonists as needed for symptoms.</p> <p>Intensity of treatment will depend on severity of exacerbations.</p> <p>Use of short acting inhaled β<sub>2</sub>-agonists more than twice weekly may indicate need for long term control therapy.</p>            |
| <b>Step 2 Mild Persistent</b>   |  |   |
| <ul style="list-style-type: none"> <li>■ Symptoms &gt; 2 times per week but &lt; 1 time per day</li> <li>■ Exacerbations may affect activity</li> <li>■ Night time asthma symptoms &gt; 2 times per month</li> <li>■ PEF or FEV<sub>1</sub> ≥ 80% predicted; PEF –variability 20%-30%</li> </ul>  | <p><b>Preferred treatment:</b> Low dose inhaled corticosteroids.</p> <p><b>Alternative treatment:</b> Cromolyn, nedocromil or leukotriene modifier or sustained-release theophylline to serum concentration of 5-15 mcg/ml.</p>  | <p>Short acting inhaled β<sub>2</sub>-agonists as needed for symptoms.</p> <p>Intensity of treatment will depend on severity of exacerbations.</p> <p>Daily use of short acting inhaled β<sub>2</sub>-agonists, or increasing use, indicates need for additional long term control therapy.</p> |
| <b>Step 3 Moderate Persistent</b>   |  |   |
| <ul style="list-style-type: none"> <li>■ Symptoms daily</li> <li>■ Exacerbations ≥ 2 times per week; may last days</li> <li>■ Night time asthma symptoms &gt; 1 time per week</li> <li>■ Daily use of inhaled short acting β<sub>2</sub>-agonist</li> <li>■ PEF or FEV<sub>1</sub> &gt;60% - &lt;80% predicted; PEF –variability &gt; 30%</li> </ul>          | <p><b>Preferred treatment:</b> Low to medium dose inhaled corticosteroid and long acting inhaled β<sub>2</sub>-agonists.</p> <p><b>Alternative treatment:</b> Increase inhaled corticosteroids within medium dose range or low to medium dose inhaled corticosteroids and either leukotriene receptor antagonist [i.e., Zafirlukast (Accolate®) or Montelukast (Singulair®)] or long acting bronchodilator (i.e., Theophylline).</p> <p>If needed, for recurring severe exacerbation, preferred treatment: increase inhaled corticosteroids within medium-dose range and add long acting inhaled β<sub>2</sub>-agonists. Alternative treatment: increase inhaled corticosteroids within medium dose range and add either leukotriene modifier or theophylline.</p> | <p>Short acting inhaled β<sub>2</sub>-agonist as needed for symptoms.</p> <p>Intensity of treatment will depend on severity of exacerbation.</p> <p>Daily use of short acting inhaled β<sub>2</sub>-agonists, or increasing use, indicates need for additional long term control therapy.</p>   |
| <b>Step 4 Severe Persistent</b>   |  |   |
| <ul style="list-style-type: none"> <li>■ Continual symptoms</li> <li>■ Frequent exacerbations</li> <li>■ Frequent night time asthma symptoms</li> <li>■ Physical activities limited by asthma symptoms</li> <li>■ PEF or FEV<sub>1</sub> ≤60% predicted; PEF –variability &gt; 30%</li> </ul>   | <p><b>Preferred treatment:</b> High dose inhaled corticosteroids AND long acting inhaled β<sub>2</sub>-agonists AND if needed, oral corticosteroids.</p>   | <p>Short acting inhaled β<sub>2</sub>-agonists as needed for symptoms. Intensity of treatment will depend on severity of exacerbations.</p> <p>Daily use of short acting inhaled β<sub>2</sub>-agonists, or increasing use, indicates need for additional long term control therapy.</p>        |

- ✓ Avoid or control triggers
- ✓ Patients should start treatment at the step most appropriate to the initial severity of their condition
- ✓ A rescue course of systemic corticosteroids may be needed at any time and at any step

# Stepwise Approach for Managing Asthma During Pregnancy and Lactation: Treatment

| Classify Severity:<br>Clinical Features Before<br>Treatment or Adequate Control  | Long-Term Control   | Quick Relief  |
|--|---|---|
| <b>Step 1 Mild Intermittent</b>  |   |   |
| <ul style="list-style-type: none"> <li>■ Symptoms <math>\leq 2</math> days/week</li> <li>■ Night time asthma symptoms <math>\leq 2</math> nights/month</li> <li>■ PEF or FEV<sub>1</sub> <math>\geq 80\%</math> predicted; PEF variability <math>&lt; 20\%</math></li> </ul>                               | <ul style="list-style-type: none"> <li>■ No daily medication needed.</li> <li>■ Severe exacerbations may occur, separated by long periods of normal lung function and no symptoms. A course of systemic corticosteroid is recommended.</li> </ul>   | <p>Use of short-acting inhaled <math>\beta 2</math>-agonist<sup>†</sup> <math>&gt; 2</math> times a week may indicate the need to initiate long-term-control therapy.</p> <p>Short-acting inhaled <math>\beta 2</math>-agonist<sup>†</sup> as needed for symptoms.</p> <p>Intensity of treatment will depend on severity of exacerbation. Course of systemic corticosteroid may be needed.</p> <p>Daily use of short-acting inhaled <math>\beta 2</math>-agonist<sup>†</sup>, or increasing use, may indicate the need to increase long-term-control therapy.</p> |
| <b>Step 2 Mild Persistent</b>  |   |   |
| <ul style="list-style-type: none"> <li>■ Symptoms <math>&gt; 2</math> days/week but <math>&lt;</math> daily</li> <li>■ Night time asthma symptoms <math>&gt; 2</math> nights/month</li> <li>■ PEF or FEV<sub>1</sub> <math>\geq 80\%</math> predicted; PEF variability <math>20\% - 30\%</math></li> </ul> | <p><b>Preferred treatment:</b> low-dose inhaled corticosteroid.*</p> <p><b>Alternative treatment</b> (listed alphabetically): cromolyn, leukotriene receptor antagonist<sup>†</sup> OR sustained-release theophylline to serum concentration of 5-12 mcg/mL.</p>  | <p>Short-acting inhaled <math>\beta 2</math>-agonist<sup>†</sup> as needed for symptoms.</p> <p>Intensity of treatment will depend on severity of exacerbation. Course of systemic corticosteroid may be needed.</p> <p>Daily use of short-acting inhaled <math>\beta 2</math>-agonist<sup>†</sup>, or increasing use, may indicate the need to increase long-term-control therapy.</p>   |
| <b>Step 3 Moderate Persistent</b>  |   |   |
| <ul style="list-style-type: none"> <li>■ Symptoms daily</li> <li>■ Night time asthma symptoms <math>&gt; 1</math> night/week</li> <li>■ PEF or FEV<sub>1</sub> <math>&gt; 60\% - &lt; 80\%</math> predicted; PEF variability <math>&gt; 30\%</math></li> </ul>   | <p><b>Preferred treatment:</b> EITHER low-dose inhaled corticosteroid* and long-acting inhaled <math>\beta 2</math>-agonist OR medium-dose inhaled corticosteroid.* If needed, (particularly in patients with recurring severe exacerbations): medium-dose inhaled corticosteroid* and long-acting inhaled <math>\beta 2</math>-agonist.</p> <p><b>Alternative treatment:</b> low-dose inhaled corticosteroid* and either theophylline or leukotriene receptor antagonist.<sup>†</sup> If needed: medium-dose inhaled corticosteroid* and either theophylline or leukotriene receptor antagonist.<sup>†</sup></p> | <p>Short-acting inhaled <math>\beta 2</math>-agonist<sup>†</sup> as needed for symptoms.</p> <p>Intensity of treatment will depend on severity of exacerbation. Course of systemic corticosteroid may be needed.</p> <p>Daily use of short-acting inhaled <math>\beta 2</math>-agonist<sup>†</sup>, or increasing use, may indicate the need to increase long-term-control therapy.</p>   |
| <b>Step 4 Severe Persistent</b>  |   |   |
| <ul style="list-style-type: none"> <li>■ Continual symptoms</li> <li>■ Frequent night time asthma symptoms</li> <li>■ PEF or FEV<sub>1</sub> <math>\leq 60\%</math> predicted; PEF variability <math>&gt; 30\%</math></li> </ul>   | <p><b>Preferred treatment:</b> High-dose inhaled corticosteroid AND long-acting inhaled <math>\beta 2</math>-agonist AND, if needed, oral corticosteroids.</p> <p><b>Alternative treatment:</b> high-dose inhaled corticosteroid* AND sustained release theophylline to serum concentration of 5-12 mcg/mL.</p>   | <p>Short-acting inhaled <math>\beta 2</math>-agonist<sup>†</sup> as needed for symptoms.</p> <p>Intensity of treatment will depend on severity of exacerbation. Course of systemic corticosteroid may be needed.</p>  |

\* There are more data on using budesonide during pregnancy than on using other inhaled corticosteroids.

† There are minimal data on using leukotriene receptor antagonists in humans during pregnancy, although there are reassuring animal data submitted to FDA.

‡ There are more data on using albuterol during pregnancy than on using other short-acting inhaled  $\beta 2$ -agonists.

### Step down:

- Review treatment every 1 to 6 months
- A gradual stepwise reduction in treatment may be possible

### Step up:

First

- Review patient medication technique
- Medication adherence
- Environmental control (avoidance of allergens and other factors that contribute to asthma)

If control is not maintained, consider step up

### Prevention (refer to Preventive Service Guidelines):

- Influenza vaccine
- Pneumococcal vaccine

### Adapted from:

National Asthma Education and Prevention Program. Expert Panel Report: *Guidelines for the Diagnosis and Management of Asthma - Update on Selected Topics 2002*. National Institutes of Health Pub. no. 02-5074. Bethesda, MD. June 2003.

National Heart Lung and Blood Institute, National Asthma Education and Prevention Program. Expert Panel Report 2: *Guidelines for the Diagnosis and Management of Asthma*. National Institutes of Health Pub. no. 97-4053. Bethesda, MD. October 1997.

National Asthma Education and Prevention Program. *Quick Reference from the Working Group Report: Managing Asthma During Pregnancy: Recommendations for Pharmacologic Treatment – Update 2004*. National Institutes of Health Pub. no. 05-5246. January 2005.

