

Asthma

**Asthma
Guideline Team**

Team Leader

Sean K Kesterson, MD
General Medicine

Team Members

- Joyce E Kaferle, MD
Family Medicine
- Jill A Noble, MD
General Pediatrics
- Manuel Arteta, MD
Pediatric Pulmonology
- Alan P Baptist, MD, MPH
Allergy & Clinical Immunology
- James A Freer, MD
Emergency Medicine
- Cyril M Grum, MD
Pulmonary & Critical Care Medicine
- Cary E Johnson, Pharm.D.
College of Pharmacy
- R Van Harrison, PhD
Medical Education

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**UMMC Guidelines
Oversight Team:**

Connie J Standiford, MD
William E Chavey, MD
R Van Harrison, PhD

For more information call:
GUIDES 734-936-9771

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These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

Patient population: Pediatric and adult.

Objectives: Provide evidence-based guidance to improve the patient's quality of life by controlling asthma symptoms at rest and during exercise, attaining normal lung function, and minimizing adverse drug reactions; preventing exacerbations; attaining normal activity levels, including exercise; and preventing unscheduled office visits, emergency visits, hospitalizations, and premature death.

Key Points (See Table 1 for overview of care for chronic asthma)

- **A high index of suspicion** for asthma is essential. A history of both symptoms and symptom triggers should be obtained. [IC*]
- **Diagnosis** is *clinical* in young children and may include *both* clinical features and lung function test results in older children and adults [IC].
- **Objective evaluation of airflow obstruction** (spirometry) should be used in the diagnosis, classification, and management of the disease in older children and adults [IC].
- **Patient education** should emphasize increasing knowledge of the disease process and active participation in treating asthma; *self-management is fundamental* to successful therapy.
 - **Structured education.** A structured asthma education program should be considered [IIB].
 - **Triggers.** Identify and avoid environmental triggers (including smoking & passive smoke) [IA].
 - **Monitoring.** All patients should be able to identify signs and symptoms of active disease, and if indicated monitor peak expiratory flow rates (PEFR). Patients with severe asthma and whose perception of their symptoms is poor, should measure their PEFR at home [IID], compare it to their personal best peak flow, and modify therapy or seek help as indicated [IA]. For other patients, symptom monitoring may be sufficient and preferable to self-measuring PEFR [IA].
 - **Asthma Action Plan (AAP).** Provide an easy to understand written AAP to patients with persistent asthma [IA]. An AAP is often useful for patients with intermittent asthma [IID].
- **Type of asthma, initial severity and follow-up level of control determine asthma treatment.** Type: intermittent or persistent. If persistent, severity: mild, moderate, or severe. Level of control: well controlled, not well controlled, or very poorly controlled.
- **Drug therapy should focus on long-term suppressive therapy in persistent asthma.**
 - **Anti-inflammatory agents** (esp. inhaled corticosteroids) are the cornerstone of this approach [IA].
 - **Short-acting beta-agonists** (SABA) are for symptom based “rescue” [IB]. Frequent use indicates poor disease control. The exception is planned use to prevent Exercise-Induced Bronchospasm.
 - **Long-acting beta-agonists** (LABA) are used in combination with inhaled corticosteroids [IA].
- **Special circumstances** addressed in the guideline include pregnancy and breast feeding, preparation for surgery, and complementary/alternative treatment.

* **Strength of recommendation:**

I = generally should be performed; II = may be reasonable to perform; III = generally should not be performed.

Levels of evidence for the most significant recommendations

A= randomized controlled trials; B= controlled trials, no randomization; C= observational trials; = opinion of expert panel

Clinical Background

**Clinical Problem
and Management Issues**

- Criteria for diagnosis of asthma are not reliably understood, and effectively applied. Asthma is often simultaneously under diagnosed and diagnosed inaccurately.
- Some patients’ ability to perceive the severity of their symptoms is poor, resulting in treatment delay.
- Asthma morbidity and mortality are unnecessarily high. Racial, ethnic, and socio-economic differences contribute to disparities in outcomes, including excess mortality.
- Care relies on perception of symptoms. Objective data should be used in diagnosis, care, and follow-up.
- Airway inflammation is a principal factor in asthma airway obstruction. Therapeutic agents to prevent or reverse this abnormality are first-line therapy in *persistent* asthma.
- Delivering high quality asthma care includes asthma education, implementation of self management processes, and the use of asthma action plans.

(Text continues on page 9)

Table 1. Overview of Diagnosis and Management of Patients with Asthma

Diagnosis

Clinical suspicion. Recurrent cough, wheezing, or shortness of breath (See symptoms and signs in Table 2.)

Trial. Symptoms/clinical signs improved or relieved by trial of SABA (adequate evidence for diagnosis *in younger children*)

Test. Additionally, in *older children and adults not on asthma medications*, FEV1/FVC may be reduced and FEV1 (forced expiratory volume in 1 second) may be < 80% normal with an increase in FEV1 ($\geq 12\%$ and 200ml) post bronchodilator. Bronchoprovocation testing (methacholine challenge) is more useful to rule out asthma than to confirm it.

Alternative diagnoses. If both trial and test are negative or equivocal, consider alternative diagnoses (see Table 3) and/or referral to an asthma specialist.

Asthma type and severity. Use the following factors to classify asthma as Intermittent or Persistent; if Persistent, classify as mild, moderate or severe. (See values in Table 6.) Overall severity is based on the most severe impairment for any factor.

- Symptoms – frequency
- Nighttime awakenings – frequency
- Interference with normal activity – extent
- Short-acting beta-2 agonist use for symptom control – frequency
- FEV1 or peak expiratory flow rate(PEFR) – % of predicted or of personal best (for older children and adults)
- FEV1/FVC – % of predicted (for older children and adults)
- Exacerbations requiring oral or parenteral systemic corticosteroids – frequency and severity

New patient with a previous diagnosis of asthma. See ongoing management discussion below.

Initial Management

Asthma explanation. Provide patient initial educational overview of asthma mechanisms, how it is diagnosed, types of asthma and severity, triggers, and treatment options (first part of Table 4).

Environmental control. Identify and review how to avoid triggers and exposures known to aggravate asthma (see Table 5).

Determine medical therapy. Determine medical therapy based on asthma type and severity by age – see Table 7. Tables 8 and 9 provide dose and cost information for medications for chronic and for acute exacerbation, respectively. Review technique for use of inhaled medication.

Asthma Action Plan (AAP). Develop a medication plan with patient/family that is fully understood (see Table 4) and agreed to. The plan should address current medical therapy, peak expiratory flow rate (PEFR) measurement (if indicated), warning symptoms/signs, medications for control and rescue, and how and when to contact a medical provider during an asthma exacerbation. Provide a written AAP to all patients with asthma. Examples of written AAPs by age group are presented in the Appendix. Place a written copy of the plan in the patient record and provide a copy to the patient/family to use at home in self management.

Prevention. Flu vaccine for all patients age 6 months or older. All adults with asthma should receive a pneumococcal vaccine.

Follow-up. Assess within 2 to 6 weeks of initial management visit.

Ongoing Management

Assess asthma control. Reassess factors used to classify type and severity (see above). Classify the patient as “well controlled,” “not well controlled,” or “very poorly controlled” using the values by age in Table 9. (Perform spirometry for older children and adults at least every 1-2 years to check function, although clinical outcome data are not available.)

Environmental control. Follow up on avoidance of triggers/ environmental and tobacco smoke exposure.

Review medical therapy.

- For “well controlled” patients: maintain current therapy or, if well controlled for 3 months, consider “step down” in therapy (see Table 7).
- For “not well” or “very poorly” controlled patients: “step up” therapy (see Table 7)

Asthma Action Plan. Review patient’s understanding (see Table 4) and/or revise AAP with patient/family at least annually.

Prevention. Annual Flu vaccine for all patients age 6 months or older. For adults, initial pneumococcal vaccination, if not already received; a 2nd dose is indicated for patients age 65 or older if their 1st dose was before age 65 and more than 5 years ago.

Consider referral. Consider referral to asthma specialist if the patient either:

- Is not well controlled within 3–6 months using stepwise approach
- Has two or more emergency department visits or hospitalizations for asthma in a year

Follow-up.

- “Well controlled” patients: reassess every 3–12 months (if stepped-down therapy, reassess in 3 months)
- “Not well” or “very poorly” controlled patients (stepped-up therapy): reassess in 2–6 weeks

Table 2. Symptoms and Signs Supporting Diagnosis of Asthma

Symptoms	Signs / Physical Exam Findings
Cough	Evidence of bronchial obstruction:
Recurrent episodes of wheezing	Wheezing
Shortness of breath or chest tightness	Prolonged expiration
Nocturnal cough	Airway obstruction at least partially reversible
Exercise induced cough or wheezing	Evidence of atopy:
Onset of symptoms after exposure to airborne allergens or other stimuli	Nose / Eyes:
History of respiratory tract infections with lingering cough	Swollen, discolored nasal mucosa
Conditions associated with asthma (eg atopic dermatitis, rhinitis, etc)	Clear nasal discharge
	Partial nasal airway obstruction
	Erythematous conjunctiva, palpebral cobblestoning, tearing
	Skin: Atopic dermatitis

Table 3. Alternative Diagnoses to Consider

Children			Adults
<u>Large Airways</u>	<u>Small airways</u>	<u>Other</u>	
Foreign body	Viral or obliterative bronchiolitis	Allergic rhinitis	Chronic obstructive pulmonary disease
Vocal cord dysfunction	Cystic fibrosis	Sinusitis	Heart failure
Vascular ring	Bronchopulmonary dysplasia	Swallowing dysfunction with aspiration	Pulmonary embolism
Laryngeal web	Heart disease	GERD	Tumor
Laryngotracheomalacia			Foreign body
Tracheal stenosis			Eosinophilic infiltration of the lung
Bronchostenosis			Vocal cord dysfunction
Enlarged lymph nodes			Medications (i.e. ACE inhibitors)
Tumor			GERD

Table 4. Patient Education Overview

<p><u>Mechanisms.</u> Two major components of asthma: broncho-spasm and inflammation.</p> <p><u>Triggers.</u> What triggers their asthma flare (e.g., viral URI, environmental allergens, exercise, cold, tobacco smoke exposure, stress). How to avoid triggers or self-medicate to prevent predictable exacerbations.</p> <p><u>Signs.</u> Their own warning signs (e.g., increased shortness of breath, chest tightness, or cough).</p> <p><u>Medications.</u> Dosing, schedule, rationale (effect on asthma mechanisms).</p> <p><u>Metered dose inhaler use.</u> How to correctly use a metered dose inhaler and spacer. (Valved holding chamber must be used in children, avoid open spacers)</p> <p><u>Peak flow meter use.</u> How to use a peak flow meter and how to interpret the results.</p> <p><u>Acute exacerbation.</u> What constitutes an acute exacerbation and what to do in such circumstances. How to self-medicate to initiate treatment of flares.</p>

Table 5. Common Asthma Triggers

Smoking (or passive smoking)	Pollutants:	Respiratory tract infections:
Indoor allergens:	Air pollutants	Viral URI illnesses
House dust mites	Occupational exposures	Sinusitis
Animal dander	Medications:	Bronchitis
Cockroaches	β-blockers	Medical comorbidities:
Molds	Aspirin	GERD
Outdoor allergens:	NSAIDs	Depression/stress
Pollens	Exercise	Rhinitis
Molds	Cold air	
	Sulfites	

Table 6. Classification of Initial Asthma Severity and Recommended Action

(The classification of severity is based on the most severe impairment or risk category.)

Patient Age	Components of Severity	Intermittent	Persistent		
			Mild	Moderate	Severe
0 – 4 years	Symptoms (e.g., wheezing, shortness of breath, chest tightness)	≤ 2 days/week	> 2 days/ week but not daily	Daily	Throughout day
	Nighttime awakenings with breathing problem	0	1-2x/month	3-4x/month	> 1x/week
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	If prescribed short-acting beta ₂ -agonist (SABA), use for symptom control	≤ 2 days/week	> 2 days/week but not daily	Daily	Several times a day
	Exacerbations requiring oral corticosteroids ¹	≤ 1x/year	≥ 2x in 6 months or ≥ 4 wheezing episodes/year lasting > 1 day AND risk factors for persistent asthma		
5 years & older	Symptoms (e.g., wheezing, shortness of breath, chest tightness)	≤ 2 days/week	> 2 days/ week but not daily	Daily	Throughout day
	Nighttime awakenings with breathing problem	≤ 2x/month	3-4x/month	> 1x/week but not nightly	Often 7x/week
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	If prescribed short-acting beta ₂ -agonist (SABA), use for symptom control	≤ 2 days/week	> 2 days/week but not daily	Daily	Several times a day
	Exacerbations requiring oral corticosteroids ¹	≤ 1x/year	≥ 2x/year ----->		
	Lung function tests ² :				
	FEV ₁ (predicted) or PEF (personal best)	> 80%	> 80%	60-80%	< 60%
FEV ₁ /FVC ³					
5 – 11 yrs	> 85%	> 80%	75-80%	< 75%	
≥ 12 yrs	Normal	Normal	Reduced 5%	Reduced > 5%	
Recommended Medical Treatment/Action⁴	Step 1	Step 2	Step 3*	0-4 yr: Step 3* 5-11 yr: Step 3/4* ≥ 12 yr: Step 4/5*	

* Consider short course of oral corticosteroids

Adapted from 2007 NHLBI Guidelines for the Diagnosis and Treatment of Asthma Expert Panel Report 3

¹ Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category.

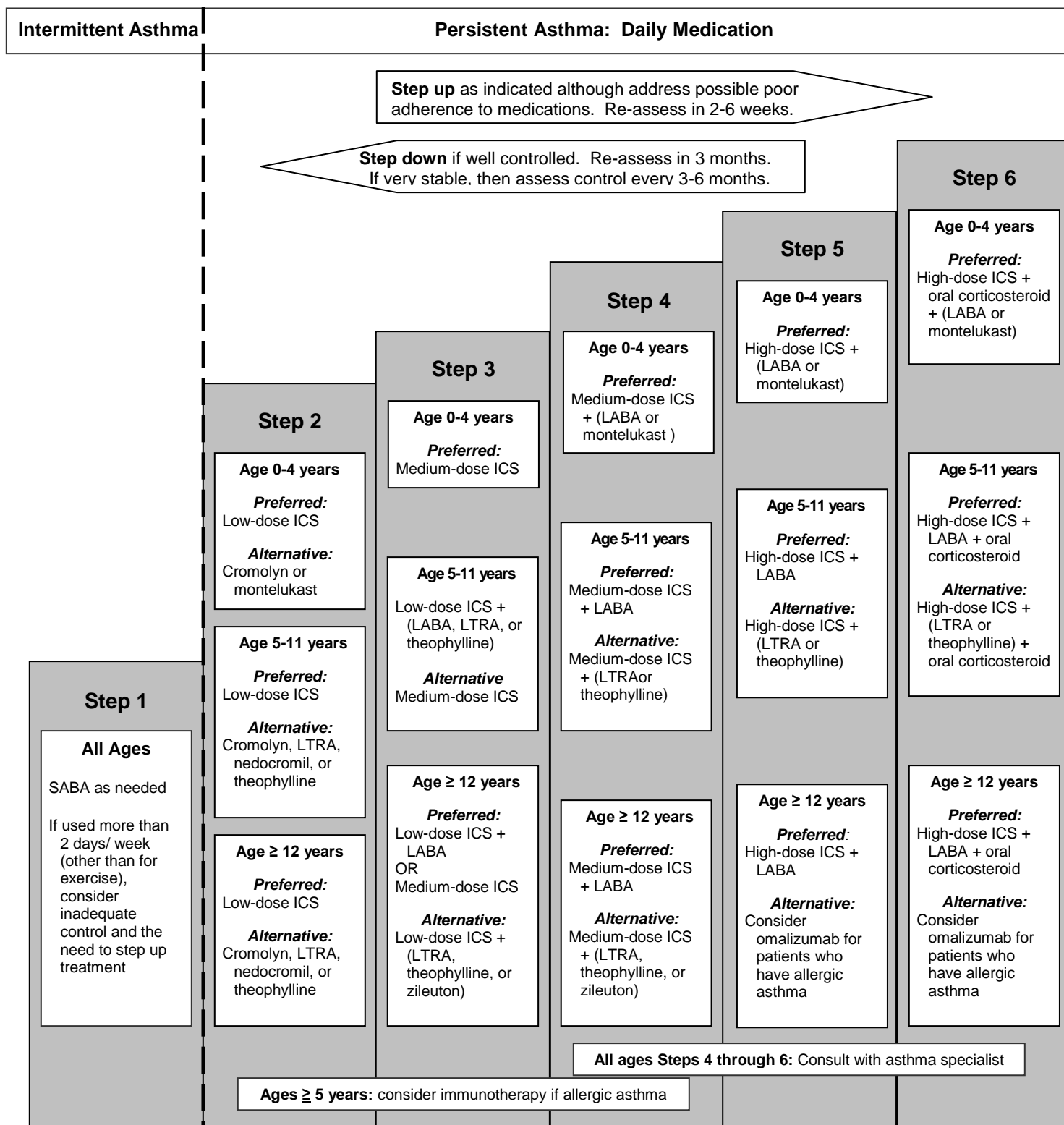
Relative annual risk of exacerbations may be related to FEV₁.

² Normal FEV₁ between exacerbations. FEV₁ = forced expiratory volume in 1 second, FVC = forced vital capacity, PEF = peak expiratory flow.

³ Normal values by age: 12-19 >85%, 20-39 >80, 40-59 >75%, 60-80 >70%

⁴ See Table 7 for the stepwise approach to medical management. Before stepping up therapy, review medication adherence, inhaler technique, environmental control, and comorbid conditions. If an alternative treatment option was used in a step, discontinue and use the preferred treatment for that step. When selecting medications, consider risks for reduction in lung growth, loss of lung function, and treatment-related adverse effects.

Table 7. Stepwise Approach to Treatment of Asthma



Note: Adapted from 2007 NHLBI Asthma Expert Panel Report 3. For initial treatment, see Table 6. For follow up treatment, see Table 9.

ICS = inhaled corticosteroid, LABA = long-acting beta-agonist, LTRA = leukotriene receptor antagonist, SABA = short-acting beta-agonist

If an alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.

Theophylline requires serum concentration levels monitoring; zileuton requires liver function monitoring.

Rescue medication: (a) SABA as needed for symptoms. Treatment intensity depends on severity. For age ≥ 5 years, up to 3 treatments at 20-min. intervals initially. For age 0-4 years with viral respiratory symptoms, every 4-6 hours up to 24 hours (longer with consult). (b) Consider short course of oral corticosteroids. (c) Increasing/frequent use of short acting beta-agonists (for age ≥ 5, > 2 days/week for symptoms [not exercise-induced]) generally indicates inadequate control and the need to step treatment.

Table 8. Pharmacologic Therapy for Chronic Asthma

Generic Name (Brand name)	Strength	Usual Pediatric Dose 0-4 Years Old	Usual Pediatric Dose 5-11 Years Old	Usual Adult Dose ≥ 12 Years	Cost for 30 day Supply ¹
Short acting β₂-adrenergic agonists (SABA) – Inhaler [bronchodilator]					
Albuterol (Proventil [HFA]) (Ventolin [HFA]) (Proair [HFA])	MDI 90 mcg/ puff	2 puffs q 4-6 hrs prn	2 puffs q 4-6 hrs prn	2 puffs q 4-6 hrs prn	\$34 - \$39
Albuterol Nebulizer solution (ProventilAccuNeb) (preservative free)	0.5% (5mg /mL)	0.15-0.25 mg/kg (minimum: 1.25 mg; maximum: 5 mg) q 4-6 hrs prn	0.15-0.25 mg/kg (minimum: 1.25 mg; maximum: 5 mg) q 4-6 hrs prn	1.25-5 mg q 4-6 hrs prn	\$12-46
Levalbuterol (Xopenex [HFA])	MDI 45 mcg/puff	N/A	2 puffs q 4-6 hrs prn	2 puffs q 4-6 hrs prn	\$50
Levalbuterol Nebulizer solution (Xopenex)	1.25 mg/0.5 mL	0.31-1.25 mg q 4-6 hrs prn	0.31-0.63 mg q 8hr prn	0.31-0.63 mg q 8hr prn	\$190-287
Pirbuterol (Maxair Autohaler)	MDI 200 mcg/puff	N/A	2 puffs q 4-6 hrs prn	2 puffs q 4-6 hrs prn	\$56-112
Inhaled Corticosteroids ² (ICS) [anti-inflammatory]					
Beclomethasone Qvar (HFA)	Qvar (HFA) MDI 40 or 80 mcg/puff	N/A	Low Dose 80-160 Medium 160-320 High >320 Divided bid	Low Dose 80-240 Medium 240-480 High >480 Divided bid	\$45-270 \$93-186
Budesonide Pulmicort Flexhaler	DPI 90 or 180 mcg/ inhalation	N/A	Low Dose 180-360 Medium 360-720 High >720 Divided bid	Low Dose 200-540 Medium 540-1080 High >1080 Divided bid	\$99-267
Budesonide Pulmicort Respules	Nebulizer solution 0.25, 0.5 or 1 mg	Low Dose 0.25-0.5 Medium 0.5-1.0 High >1.0 Divided bid	Low Dose 0.5 Medium 1.0 High 2.0 Divided bid	N/A	\$184-866
Ciclesonide Alvesco (HFA)	MDI 80, 160 mcg/puff	N/A	N/A	Low Dose 160-320 Medium 320-640 High >640 Divided bid	\$146-292
Flunisolide Aerobid	MDI 250 mcg/puff	N/A	Low Dose 500-750 Medium 1000-1250 High >1250 Divided bid	Low Dose 500-1000 Medium 1000-2000 High >2000 Divided bid	\$58-260

Table continues on next page

MDI= Metered Dose Inhaler; DPI = Dry Powder Inhaler; HFA= approved propellant; VHC=Valved Holding Chamber

¹ Cost = Average wholesale price based -10% for brand products and Maximum Allowable Cost (MAC) + \$3 for generics on 30-day supply, Amerisource Bergen item catalog, 5/09, and Michigan Department of Community Health M.A.C. Manager, 5/09

² High doses of inhaled steroids may have significant side effects; see text for discussion.

Table 8. Pharmacologic Therapy for Chronic Asthma, continued

Generic Name (Brand name)	Strength	Usual Pediatric Dose 0-4 Years Old	Usual Pediatric Dose 5-11 Years Old	Usual Adult Dose ≥ 12 Years	Cost for 30 day Supply ¹
Inhaled Corticosteroids ² (ICS) (continued)					
Flunisolide Aerospan (HFA)	MDI 80 mcg/puff	N/A	Low Dose 160 Medium 320 High >640 Divided bid	Low Dose 320 Medium 320-640 High >640 Divided bid	(Not yet available)
Fluticasone Flovent (HFA)	MDI 44, 110 or 220 mcg/puff	Low Dose 88-176 Medium 176-352 High >352 Divided bid with VHC	Low Dose 88-176 Medium 176-352 High >352 Divided bid	Low Dose 88-264 Medium 264-440 High >440 Divided bid	\$50-204
Mometasone Asmanex TwistHaler	DPI 110 or 220 mcg/puff	N/A	Low Dose 110 Medium 220-440 High >440 Daily (PM) or divided bid	Low Dose 220 Medium 440 High >440 Daily (PM) or divided bid	\$110-200
Triamcinolone Azmacort	MDI 75 mcg/puff	N/A	Low Dose 300-600 Medium >600-900 High >900 Divided bid-four times daily	Low Dose 300-750 Medium >750-1500 High >1500 Divided bid-four times daily	\$73-362
Combination: Inhaled Corticosteroids ² (ICS) + Long-Acting β-agonists (LABA)					
Budesonide/ fomoterol Symbicort (HFA)	MDI 80 mcg/4.5 mcg or 160 mcg/4.5 mcg/puff	N/A	2 inhalations bid, dose depends on level of severity or control	2 inhalations bid, dose depends on level of severity or control	\$174-198
Fluticasone/ salmeterol Advair Diskus	DPI 100 mcg/50 mcg, 250 mcg/50 mcg or 500 mcg/50 mcg/ inhalation	N/A	1 inhalation bid, dose depends on level of severity or control	1 inhalation bid, dose depends on level of severity or control	\$172-281
Fluticasone/ salmeterol Advair (HFA)	MDI 45 mcg/21 mcg, 115 mcg/21 mcg or 230 mcg/21 mcg/puff	N/A	2 inhalations bid, dose depends on level of severity or control	2 inhalations bid, dose depends on level of severity or control	\$172-281
Long-Acting β-agonists (LABAs) ³ – Inhaler [bronchodilator]					
Salmeterol Serevent Diskus	DPI 50 mcg/dose	N/A	1 dose bid	1 dose bid	\$156
Formoterol Foradil Aerolizer	DPI 12 mcg/ dose	N/A	1 capsule bid	1 capsule bid	\$150

Table continues on next page

³ The US Food and Drug Administration (FDA) requires products containing long-acting beta agonists (Advair Diskus, Serevent Diskus, Foradil Aerolizer, and Symbicort) to have a warning on their label that long-acting beta agonists may increase the chance of severe asthma episodes and asthma-related deaths and are not to be used as monotherapy or for acute asthma management..

Table 8. Pharmacologic Therapy for Chronic Asthma, continued

Generic Name (Brand name)	Strength	Usual Pediatric Dose 0-4 Years Old	Usual Pediatric Dose 5-11 Years Old	Usual Adult Dose ≥ 12 Years	Cost for 30 day Supply ¹
Leukotriene Modifiers – Oral [anti-inflammatory]					
Montelukast Singulair	4 mg, 5 mg chewable tablet 4 mg oral granules 10 mg tablet	4 mg hs Age 6 mo-5 yrs	5 mg hs Age 6-14 yrs	10 mg hs Age >14 yrs	\$117
Zafirlukast Accolate	10 mg, 20 mg tablet	N/A	10 mg bid	20 mg bid	\$100
Zileuton Zyflo	600 mg tablet	N/A	N/A	600 mg qid	\$303
Mast Cell Stabilizers – Inhaler [anti-inflammatory]					
Cromolyn sodium Intal (HFA) OTC	MDI 800 mcg/puff	N/A	2-4 puffs tid-four times daily	2-4 puffs tid-four times daily	\$77-\$252
Cromolyn sodium Intal	Nebulizer solution 20 mg/ampule	20 mg four times daily > 2 yrs	20 mg four times daily	20 mg four times daily	(Brand NA) \$72-160 (generic)
Nedocromil sodium Tilade	MDI 1750 mcg/puff	N/A	2 puffs bid-four times daily	2 puffs bid-four times daily	\$49-289
Methylxanthine ⁶ – Oral [anti-inflammatory]					
Theophylline	Controlled release tablets, capsules 100 mg, 200 mg, 300 mg, others	Starting dose 10 mg/kg/day	Starting dose 10 mg/kg/day	Starting dose 10 mg/kg/day Max: 900 mg/day for otherwise healthy, nonsmoking adults. Reduce to 400 mg for cardiac, liver disease.	\$19-60 (brand) \$12-36 (generic)
Note: 12-24 hour controlled release preferred; sprinkle beads for younger					
Theophylline Elixophylline (20% alcohol)	liquid 80 mg/15 mL	>1 year of age: 16 mg/kg/day < 1 yr: 0.2 (age in wks) + 5=mg/kg/day	>1 year of age: 16 mg/kg/day		\$48-95
Oral Corticosteroids ⁴ [anti-inflammatory] Note: dosing within age group is the same for both drugs					
Prednisone:	1, 2.5, 5, 10, 20, 25 mg tabs; 1 mg/mL liquid	0.25-2 mg/kg/day in a single, divided or every other day dose as needed for control;	0.25-2 mg/kg/ in a single, divided or every other day dose as needed for control;	7.5-60 mg/day in a single, divided or every other day dose as needed for control;	\$4-12 (generic)
Prednisolone: 1mg/mL, 3 mg/mL liquid	1mg/mL, 3 mg/mL liquid	short course burst with taper: 1-2 mg/kg/day, max 60 mg/day, for 3-10 days	short course burst with taper: 1-2 mg/kg/day, max 60 mg/day, for 3- 10 days	short-course burst 40-60 mg/day, for 3-10 days without or with taper ⁵	\$7-28 (2 oz generic liquid) \$12-50 (2 oz. brand liquid)

⁴ If patients are started on inhaled corticosteroids, it may be necessary to slowly taper the systemic corticosteroid dose depending on dose and duration of therapy. Prednisolone (3 mg/mL) generic preferred for children due to taste.

⁵ Example of taper: start taper on day 3 – 60 mg, then day 4 – 50 mg, day 5 – 40 mg, day 6 – 30 mg, day 7 – 20 mg, day 8 – 10 mg, day 9 – off.

⁶ Dosage adjustments of oral theophylline are based on a trough serum concentration obtained at steady state

Table 9. Classification of Follow-Up Level of Control and Recommended Action

(The classification of control is based on the most severe impairment or risk category.)

Patient's Age	Components of Control	Well Controlled	Not Well Controlled	Very Poorly Controlled
0 – 4 years	Symptoms: (e.g., wheezing, shortness of breath, chest tightness)	≤ 2 days/week but ≤1x/day	> 2 days/week or multiple times on ≤ 2 days/week	Throughout the day
	Nighttime awakenings with breathing problem	≤ 1x/month	> 1x/month	> 1x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	SABA used for symptom control ¹	≤ 2 days/week	> 2 days/week	Several times/day
	Exacerbations requiring oral corticosteroids ²	≤ 1 time/year	2-3x/year	> 3x/year
5 – 11 years	Symptoms: (e.g., wheezing, shortness of breath, chest tightness)	≤ 2 days/week but ≤1x/day	> 2 days/week or multiple times on ≤ 2 days/week	Throughout the day
	Nighttime awakenings with breathing problem	≤ 1x/month	≥ 2x/month	≥ 2x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	SABA used for symptom control ¹	≤ 2 days/week	> 2 days/week	Several times per day
	Exacerbations requiring oral corticosteroids ²	≤ 1 time/year	≥ 2x/year	≥ 2x/year
	Lung function tests ³ :			
	FEV ₁ (predicted) or PEF (personal best)	> 80%	60-80%	< 60%
FEV ₁ /FVC	> 80%	75-80%	< 75%	
≥ 12 years	Symptoms: (e.g., wheezing, shortness of breath, chest tightness)	≤ 2 days/week	> 2 days/week	Throughout the day
	Nighttime awakenings with breathing problem	≤ 2x/month	1-3x/ week	≥ 4x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	SABA used for symptom control ¹	≤ 2 days/week	> 2 days/week	Several times per day
	Exacerbations requiring oral corticosteroids ²	≤ 1 time/year	≥ 2x/year	≥ 2x/year
	Lung function tests ³ :			
	FEV ₁ (predicted) or PEF (personal best)	> 80%	60-80%	< 60%
	Questionnaires ⁴ :			
	ATAQ	0	1-2	3-4
	ACQ	≤ 0.75	≥ 1.5	n/a
ACT	≥ 20	16-19	≤ 15	
Recommended Medical Treatment/Action ⁵		Maintain current step; consider stepping down if well controlled for ≥ 3 months	Step up 1 step	Step up 1-2 steps and consider short course of oral corticosteroids

Adapted from 2007 NHLBI Guidelines for the Diagnosis and Treatment of Asthma Expert Panel Report 3.

¹ Short-acting beta₂-agonist (SABA)² Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. Relative annual risk of exacerbations may be related to FEV₁.³ Normal FEV₁ between exacerbations. FEV₁=forced expiratory volume in 1 second, FVC=forced vital capacity, PEF=peak expiratory flow.⁴ Validated questionnaires: ACQ=Asthma Control Questionnaire, ACT=Asthma Control Test, ATAQ=Asthma Therapy Assessment Questionnaire.⁵ See Table 7 for the stepwise approach to medical management. Before stepping up, review adherence to medication, inhaler technique, environmental control, and comorbid conditions. If an alternative treatment option was used in a step, discontinue and use the preferred treatment for that step. When selecting medications, consider risks for reduction in lung growth, loss of lung function, and treatment-related adverse effects.

Rationale for Recommendations

An overview of the diagnosis and management of asthma is presented in Table 1. The rationale for recommendations is organized according to the overview.

Diagnosis of Asthma

Steps in arriving at a diagnosis of asthma are summarized in Table 1. Each step is described in more detail below.

Clinical Suspicion: Symptoms and Signs

Symptoms. Common symptoms of asthma are cough, wheezing, shortness of breath/dyspnea, and chest tightness (Table 2). These symptoms are not always present at the same time and are not in themselves diagnostic. Recurrent symptoms, especially if provoked by exogenous factors, are very suggestive of asthma. Recurrent or prolonged isolated cough without another discernible cause is very consistent with asthma especially in young patients and non-smokers.

The diagnosis of asthma can be especially difficult in the 0-4 year old age group, especially in wheezing infants. Approximately 50% of young children will have recurrent episodes of wheezing, one third of them will eventually develop persistent/atopic wheezing, in 40 % the wheezing will be transient and in the other third the wheezing will start later in childhood. For the purpose of establishing guidelines for therapy, the young child who has more than 2 episodes of asthma symptoms (wheezing, persistent cough, etc.) in a year, regardless of the trigger, should be treated for asthma and followed carefully for response to treatment. In some children, the only symptom of asthma is cough. In this age group, diagnosis depends a great deal on clinically observable reversibility.

Other features may also help with diagnosis. The presence of atopic dermatitis or a family history of asthma are strong predictors of asthma in the symptomatic young child. The following can increase the likelihood that the chronically symptomatic child has asthma:

- Parental history of asthma
- Physician diagnosis of atopic dermatitis
- Sensitization to aeroallergens or foods
- Two of the following:
 - ≥ 4 % peripheral blood eosinophilia
 - Wheezing apart from colds.
 - Sensitization to foods

Signs. The key elements of the physical exam are the upper airway, chest/lungs and skin. The exam is aimed at finding evidence of lower airway obstruction (wheezing, intercostal retraction during inspiration, chest hyperinflation, and prolonged expiratory phase) and signs suggestive of atopy (Table 2). Because asthma is characteristically episodic and has variable severity, the chest/lung physical examination may be completely normal.

Trial of Reversibility

In young children with recurrent or prolonged wheezing, a

trial of reversibility of symptoms using a short acting β_2 -adrenergic agonist (SABA) may be diagnostic. Administer the SABA as needed for wheezing or persistent cough either by nebulizer and mask or by metered dose inhaler with valved holding chamber and mask. Close attention should be paid to any evidence of response within 15 to 20 minutes of administration and the trial should be not longer than 1-2 weeks to avoid over-administration of a medication that may not be helpful. If the SABA trial provides no relief of symptoms, alternative diagnoses for the wheeze should be considered.

A similar trial of reversibility in older children and adults is helpful clinically, and often necessary for symptom control while waiting to conduct lung function tests to confirm the diagnosis.

Testing Lung Function

Spirometry. Perception of airway obstruction in patients with asthma does not always correlate with the measured severity of obstruction (cohort studies). For this reason, an NIH expert panel recommends spirometry for diagnosing and grading the severity of asthma (expert opinion).

Bronchodilator. For adults and older children, spirometry measurements (FEV₁, FEV₁, FVC, FEV₁/FVC and FEF 25-75) ratio before and after the patient inhales a short-acting beta agonist) can document airway obstruction, demonstrate reversibility. Reversible airflow obstruction with 12% increase in FEV₁ after bronchodilator is consistent with a diagnosis of asthma.

Bronchoprovocation. A bronchoprovocation test uses methacholine and standardized protocols. A positive test indicates airway hyperresponsiveness, a characteristic feature of asthma that can also be present in other conditions. Although a positive test is consistent with asthma, a negative bronchoprovocation may be more helpful to rule out asthma.

Peak flow meter. Measurements by peak flow meter in physicians' offices should not be used to determine the diagnosis of asthma.

Previously Diagnosed Asthma

Many patients with previously diagnosed asthma will present to the primary care physician. If the patient has symptoms and history consistent with asthma, it is appropriate to categorize type, severity, and control, and treat accordingly. In asymptomatic patients classify severity according to the least amount of medication that controls their symptoms. Provide care as described in Table 1 under "Ongoing Management". Performing lung function tests before and after step down of treatment may help clarify the accuracy of prior diagnosis.

Exclusion of Alternative Diagnoses

All of the symptoms of asthma can be caused by other airway or parenchymal conditions (Table 3). When the

diagnosis is in doubt or specialized testing is required, referral to a specialist in asthma care would be appropriate.

Differentiating asthma from emphysema and chronic obstructive pulmonary disease (COPD) (or their comorbid presence with asthma) is of great importance in older patients with a history of smoking affecting management and prognosis. Features likely to differentiate between asthma and COPD are listed in Table 10, below.

Some patients have an overlap of these two syndromes. Some COPD patients may have a small amount of obstruction that is *partially* reversible. If overlapping syndromes are suspected, consider referral to a specialist for a recommendation concerning best management options for the specific patient.

Table 10. Factors Differentiating Asthma and COPD

<u>Asthma</u>	<u>COPD</u>
Onset at early age	Tobacco use history (90% of patients with COPD have smoked)
Family history of asthma	
Personal history of atopy	Onset at older age
Nocturnal symptoms	Obstruction not reversible in lung function test
Reversible obstruction in lung function test	

Assess Asthma Severity

Asthma severity is classified as intermittent or persistent, and within persistent classified as mild, moderate, or severe. Classification at time of diagnosis is based on symptoms, night time awakenings, frequency of use of short-acting beta-agonist, interference with normal activity, lung function, and exacerbations requiring oral corticosteroids. Table 6 presents values on each of these factors by classification. As shown at the bottom of Table 6, the classification is used to determine initial medical therapy. The classification of severity after asthma is treated and controlled is based on the lowest level of treatment required to maintain control.

Initial Asthma Management

Steps in the initial management of asthma are outlined in the second section of Table 1 and are detailed below.

Asthma Explanation

Educate patients and care givers about asthma, medications and inhaler use monitoring, and exacerbations. Key educational points to address include:

- Asthma mechanisms: inflammation and bronchospasm
- The Asthma Action Plan (AAP)
- Triggers, Environmental Exposures
- Proper inhaler and device use
- Warning symptoms/signs

- Peak expiratory flow rate (PEFR) if indicated
- Controller vs. rescue medications

Education can and should be done at all asthma visits, and by many members of the health care team. Severe asthma patients (especially children) benefit from comprehensive educational programs. See Table 4 for a reminder list of educational points, described in more detail below. Patient education materials about asthma and its control are available at www.med.umich.edu/1info/fhp/practiceguides/.

The basic disease process of inflammation, with precipitated bronchospasm should be explained. This can naturally lead to discussions about triggers and controller versus rescue medications, and symptom and peak flow monitoring. It is important to discuss inhaler technique, including the recommended use of spacers, valved holding chambers, and breath activated inhalers, as well as nebulizers. Dose counting charts are available to help patients make sure they are using inhalers containing active drug. Information on using a metered dose inhaler (MDI), instructions for specific devices, and an MDI dose tracking sheet are available at www.med.umich.edu/1info/fhp/practiceguide.

For exacerbations, early treatment is the best strategy. The principal goal of treatment is rapid reversal of airflow obstruction. This is best accomplished by repetitive treatment with an inhaled β_2 -agonist if needed. Early administration of systemic corticosteroids should be done in patients with severe attacks or in patients who fail to respond promptly and completely to an inhaled β_2 -agonist.

Environmental Control

Asthma triggers can either induce airway inflammation or precipitate acute bronchospasm (Table 5). The majority of asthmatics are atopic, especially in the pediatric age group. In atopic asthmatics, aeroallergen exposure and sensitivity contribute significantly to the development and persistence of asthma.

Patients with persistent asthma should be evaluated for the role of allergens as contributing factors, since success with allergen avoidance is predicated on accurate identification of the offending allergens. A combination of the patient's medical history and skin or *in-vitro* testing is the only reliable way to determine sensitivities to allergens. Skin testing correlates with bronchial allergen challenge and can, in many instances, identify controllable environmental allergens. Allergen immunotherapy should be considered for patients with persistent asthma if there is a clear relationship between symptoms and exposure to an allergen to which the patient is sensitive.

Environmental tobacco smoke. Some patients with asthma continue to smoke. Smoking cessation for these patients is a critical first step in reducing inflammation. Cessation of smoking should be strongly advised for parents of children with asthma. Smoking has been shown to impair the short term response to both systemic and inhaled corticosteroids.

Exposure to second hand smoke can trigger asthma attacks or worsen lung function. Query patients about their exposure to second hand smoke, and recommend avoidance if possible. High-efficiency particulate air (HEPA) filters can reduce the level of particulate tobacco smoke.

Indoor allergens. Because a large portion of any 24-hour period is spent in the bedroom, the most important continuous source of indoor allergen exposure comes from this room. The workplace is another important source of indoor allergen exposure.

House dust mites are microscopic arachnids (spider family) that live in mattresses, bedding, furniture, and carpets. They thrive in high humidity and eat dead skin cells. High levels of mites can be found in dust from mattresses, pillows, carpets, upholstered furniture, bed covers, clothes, and soft toys. Effective mite control measures include washing bedding materials in hot water to denature mite allergens ideally every week. Encasing the mattress, pillows and box spring reduces mite allergen levels and is also recommended for mite-allergic asthmatics. Additional control measures include removing carpeting from the bedroom, reducing humidity to less than 50%, cleaning carpets once a week with a high-efficiency particulate air (HEPA) vacuum cleaner, and minimizing or washing children's stuffed bed toys. Clinical studies have shown that a single avoidance step, such as dust mite covers alone, are generally ineffective, but that a comprehensive approach can improve outcomes.

All warm-blooded pets--including cats, dogs, rodents, and birds--produce allergens that can trigger asthma. Removal of animals to which the patient is allergic from the patient's environment is extremely important. The perceived benefit may not be immediate because animal allergens may linger for months after animal removal. If removal of the animal is not acceptable, the pet should be kept out of the patient's bedroom and the bedroom door should be kept closed. Removal of upholstered furniture and carpets, or isolation of the pets from these items, will also be beneficial. HEPA vacuum cleaners can reduce the airborne level of pet allergens. The role of regular washing of the allergenic pet has not been established.

Cockroaches and indoor molds are additional allergens that can trigger asthma in sensitive individuals. Measures to remove these allergens should be undertaken if possible. HEPA filters (in homes with forced air heating and cooling systems), repair of leaky pipes, and keeping humidity levels less than 50% have been shown to reduce mold spores. Poison baits or traps may be effective at removing cockroaches, though professional services may be needed.

In the workplace, there are numerous agents that have been identified as occupational allergens and irritants that can precipitate asthma. Once the worker is sensitized to a particular agent, the level of agent necessary to induce symptoms may be very low. PEFr monitoring on and off the job and Material Safety Data Sheets (required by the US Occupational Safety and Health Administration [OSHA] for

all work places) can help identify occupational triggers. Attempts to reduce occupational trigger exposure have been successful in a number of industrial settings.

Outdoor allergens. Outdoor allergens (pollens and molds) are common triggers and impossible to avoid completely. Exposure may be reduced by staying indoors, closing windows and doors and by using air-conditioning and filtering devices, especially during peak pollen times (midday and afternoon). This may not be realistic for some patients, especially children.

Food triggers. Foods are extremely rare asthma triggers. One food additive that has been substantiated as an asthma trigger is sulfites, which are common food and drug preservatives found in processed potatoes, shrimp, dried fruits, beer and wine. Patients should be queried about any association between these foods and asthma symptoms, and advised to avoid offending foods.

Indoor air pollution. Smoke from various sources (e.g., tobacco, wood stoves, or heating), aerosols, household sprays, volatile organic compounds, strong odors and scents, and air pollutants can trigger asthma. Patients should avoid these exposures accordingly.

Medications. In certain patients aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) can cause severe exacerbations. Adult patients should be queried regarding precipitation of bronchospasm by aspirin and other NSAIDs. The association is highest in those with severe persistent asthma or nasal polyps. Nonselective beta-blockers can cause asthma symptoms, though cardioselective beta-blockers can usually be tolerated.

Exercise-induced bronchospasm (EIB). During exercise, hyperventilating air that is cooler and dryer than that of the respiratory system can result in a loss of heat, water, or both from the lung. Some studies suggest that release of inflammatory mediators is involved. This process results in bronchospasm, airway obstruction, and symptoms. This process may occur in patients with either intermittent or persistent asthma. EIB may be diagnosed by a 15% decrease in FEV1 from pre- to post exercise.

Usual management approaches for asthma can be used as pretreatment to prevent inflammation. SABAs 20 minutes before exercise will prevent EIB in more than 80% of patients. Some patients may require a controller medication. leukotriene receptor antagonists (LTRAs) can attenuate EIB in up to 50% of patients, but inhaled steroids may be required. Cromolyn inhalers and oral montelukast have also demonstrated efficacy. Training and sufficient warm up also reduce the incidence and severity of exercise-induced bronchospasm.

Exercise may be the only trigger of asthma symptoms in some patients, but EIB is often a marker of uncontrolled asthma. These patients should be closely monitored to ensure that they are asymptomatic at rest. When assessing asthma control, frequent or severe episodes of EIB suggest

stepping up medication for long-term control (see Tables 6 and 9).

Infections. Viral infections are implicated in the majority of asthma exacerbations in children, and also appear to be important in adults. Respiratory syncytial virus (RSV), rhinovirus, and influenza virus have all been implicated. Bacterial infections with both *Mycoplasma* and *Chlamydia* may also contribute to exacerbation rates and disease chronicity and severity.

Concurrent medical conditions. Concurrent conditions that can exacerbate asthma include infections (e.g., viral upper respiratory infections, bronchitis, sinusitis), allergic rhinitis, gastroesophageal reflux disease, allergic bronchopulmonary aspergillosis (ABPA), obesity, obstructive sleep apnea (OSA), and stress/depression. Addressing these conditions can improve asthma control.

Initiate Medical Therapy

Medications for asthma are used to reduce airway inflammation and reverse airway obstruction (bronchodilation). Medical therapy includes a treatment approach for maintenance and for acute exacerbations.

In selecting a medication, its delivery system should be considered in the context of the patient's abilities and circumstances. Delivery systems include nebulizers, metered dose propellant inhalers, dry powder inhalers, and breath-activated inhalers. Considerations include limits of patient's (or care giver's) skills and experience and reimbursement coverage for durable medical equipment.

Approaches to medical therapy are summarized below, along with information about each class of medications and their drug delivery systems.

Stepwise approach. A stepwise approach to therapy is presented in Table 7. Evaluation of response at a step leads to the decision to reduce (step down), maintain, or increase (step up) the potency of therapy.

Classes of medications, in order of their general use in stepped therapy, are:

1. Short-acting beta agonists (SABA) [bronchodilator]
2. Inhaled corticosteroids (ICS) [anti-inflammatory]
3. Long-acting beta agonists (LABA) [bronchodilator]
4. Leukotriene receptor antagonists (LTRA) [anti-inflammatory]
5. Mast cell stabilizers and/or methylxanthines [anti-inflammatory]
6. Systemic (oral) corticosteroids [anti-inflammatory]

Initial medical therapy is determined by the initial classification of the patient's type and severity of asthma (see above and Table 6). After classifying the patient's condition on Table 6, the bottom of Table 6 indicates the step on Table 7 at which treatment should be initiated. Patients with intermittent asthma are prescribed treatment for exacerbations. Patients with persistent asthma are

prescribed "controller" medication appropriate for the severity level as well as treatment for exacerbations. As explained further below, a written asthma action plan (AAP) for the patient provides instructions for medical therapy, how to contact the physician's office, and when to seek emergency medical evaluation.

Exacerbations. Asthma symptoms may be aggravated by environmental triggers, infection, exercise, or other factors. SABAs are the "rescue" medication for exacerbations (or flares). Treatment is initiated as needed for symptoms. Treatment intensity depends on severity. Increasing frequency of SABA indicates a probable need to step-up therapy (Table 7).

For children under 5 years old, with an asthma exacerbation, patients can increase their use of a SABA to every 4-6 hours for up to 24 hours. If the treatment provides no relief or if symptoms seem to be worsening, patients should seek immediate medical advice.

In older children, in addition to the steps recommended for younger patients SABAs can be given every 20 minutes twice while the family seeks contact with the patient's medical provider. Further treatment frequency depends on severity and will require medical advice.

In adults, SABAs can be given every 20 minutes initially for one hour. Further treatment frequency depends on severity and may require medical advice.

In patients of all age groups with partial or slow response to SABA, consider prescribing a short course of oral (systemic) corticosteroids. Systemic corticosteroids have long-term side effects and are not recommended for long term maintenance.

Acute severe exacerbation of asthma. Patients may seek urgent care for an acute flare of asthma or with status asthmaticus. Aggressive pharmacologic therapy is given under clinical supervision, often in the emergency room and possibly requiring hospitalization. A detailed description of classifications and therapy for severe exacerbation is beyond the scope of this guideline, which focuses on routine care for mild exacerbations involving patient self-management. Details regarding management of severe acute exacerbations are described in the National Asthma Education and Prevention Program Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma Summary Report 2007, pages 53-57 at www.nhlbi.nih.gov/guidelines/asthma.

Classes of medications. The medications used to manage asthma are described in more detail below. Table 7 indicates classes of drugs to use for various levels of severity. Table 8 presents examples of specific drugs used for chronic asthma management, including dosing and cost.

Inhaled short-acting beta agonists (SABA) have been and remain a therapy of first choice for relief of acute symptoms and prevention of exercise-induced bronchospasm in infants, children, and adults. Frequent, and dependent use is

a clinical indicator of poorly controlled asthma, and should trigger change in the treatment plan.

Intermittent, short-acting, inhaled β_2 -agonists alone are frequently effective in controlling the symptoms of mild asthma. Occasional PRN therapy with inhaled β_2 -agonists is acceptable as long as asthma symptoms are controlled, Chronic SABA use should be avoided.

For patients experiencing difficulty with traditional MDI technique, another short-acting β_2 -agonist delivery option includes use of the Autohaler (breath-activated MDI) nebulizer. The Diskus (breath-activated dry powder inhaler [DPI]) is available when a LABA is desired. Similar to steroid DPI's, these delivery systems offer an advantage to patients who cannot coordinate activation and inhalation. Activation is, however, dependent upon a rapid, deep inhalation by the patient. Therefore these DPI delivery mechanisms are not recommended for small children.

Several epidemiologic studies have found an association between excess use of β_2 -agonist (short and long-acting) inhalers and asthma mortality. A causal relationship has not been demonstrated, and it is possible that β_2 -agonists represent a mere marker for the severity of disease, being more frequently prescribed for patients with life-threatening asthma. If β_2 -agonists do have a causative role, it may be an indirect one, such as delaying presentation until airway obstruction is more severe. While important to recognize, such an association would not necessarily mandate a change in current prescribing practices. A number of prospective studies have failed to demonstrate any alteration in airway hyper-responsiveness with chronic β_2 -agonist use. In addition, tolerance to the effects of β_2 -agonists with chronic use has been hard to demonstrate, suggesting that significant down regulation of β -receptors likely does not occur.

Inhaled corticosteroids (ICS) help control inflammation, a mainstay of therapy in persistent asthma. These medications help to reduce the airway response to allergens and irritants, and prevent repeated and dangerous exacerbations. Strong evidence from clinical trials demonstrates that inhaled corticosteroids improve outcomes in persistent asthma. The National Asthma Education Program consensus statement endorses the use of inhaled corticosteroids for all patients with persistent asthma regardless of severity.

Since inflammation plays a central role in asthma, many clinicians find that the added control achieved with chronic inhaled corticosteroids allows inhaled SABAs to be used on a PRN basis. Increasing reliance on inhaled SABAs is a marker of worsening disease or an impending severe attack and should trigger an overall reassessment and possible alteration in therapy, usually involving increased efforts to control airway inflammation.

Inhaled corticosteroids may have an adverse effect on linear growth (approximately 1 cm) in children. This effect must be balanced against the risk of poorly controlled asthma

delaying growth. The efficacy of ICSs is generally sufficient to outweigh concerns about growth or other systemic effects. Management of children requiring long term inhaled corticosteroids includes counseling on the risk of growth impairment, nutritional supplementation of vitamin D and calcium at age appropriate levels, maximizing asthma control with lowest effective dose of ICS, and monitoring linear growth.

Studies of markers of bone deposition and absorption, and of bone mineral density, suggest that osteopenia is a concern with inhaled corticosteroids in the adult population and increases with dose and duration of use. Patients who need to take medium to high doses of inhaled corticosteroids long-term may need prophylactic measures (supplemental calcium with vitamin D) to reduce the potential development of osteoporosis. For more information on assessment of risk and testing for osteoporosis, see UMHS guideline [Osteoporosis Prevention and Treatment](#).

Risk of cataracts increases with long-term use of inhaled corticosteroids. Periodic ophthalmologic exams should be considered based on dose and duration of use.

A long-acting beta-agonist (LABA) should be added to a medium dose inhaled corticosteroid before using high dose corticosteroids. This combination therapy has been shown to have more favorable outcomes than high dose steroids alone, while maintaining lower exposure to steroids.

High doses of inhaled corticosteroids may cause systemic side effects (though to a much lesser extent than oral steroids). Risk of topical and systemic side effects with high-dose inhaled steroids can be minimized by having the patient rinse his/her mouth immediately after inhalation, spit out the rinse water, and by always using a spacer device, preferably with a valved holding chamber (VHC). The VHC also reduces the amount of inhaled corticosteroid from MDIs that can be swallowed and potentially available for systemic absorption. When the VHC with a mask is used, the facial area under the mask should be washed with mild soap and water after drug administration to prevent topical adverse effects.

Dry powder inhalers are now available for select steroids (Pulmicort Flexhaler and Advair Diskus: Flovent/Serevent combination) in addition to traditional metered dose inhalers. Advantages of these devices include easier administration of doses and lack of chlorofluorocarbons. No coordination is necessary between device activation and inhalation; however, a minimal inspiratory flow rate is needed to activate the device, which may make usage difficult during exacerbations. The relative ease of use with these devices may make them more suitable for children ≥ 5 years of age and the elderly, who may experience difficulty with the MDI. Combination products, such as flovent/serevent (Advair) and budesonide/fomoterol (Symbicort) allow simplification of the medication regimen which may be especially useful for patients with compliance problems, such as adolescents. A small study evaluated dental hygiene in children 7-17 years of age before and after

1 month of salmeterol/fluticasone 100/50 DPI twice daily. The study reported a significant decrease in salivary flow and increase in dental plaque in the post-treatment group suggesting that good dental hygiene and dental checks are important in this population.

Long-acting beta agonists (LABA) are used in controlling moderate and severe persistent asthma in children (not infants) and adults.

Salmeterol and formoterol, the only LABAs currently available, demonstrate a 12-hour duration of action (5-hour with regular chronic use). Salmeterol may be used twice daily for maintenance or before bedtime for nocturnal asthma symptoms. Safety and efficacy for salmeterol has been established in children as young as 4 years of age and for formoterol as young as 5 years. Salmeterol and formoterol are not indicated for acute bronchospasm. The patient should always have a short-acting bronchodilator available for treating acute symptoms. Both agents should always be administered in combination with an anti-inflammatory agent when used for maintenance therapy. Monotherapy is only approved for exercise-induced bronchospasm on a strict intermittent basis.

A recent secondary data analysis associated use of LABAs with an increase in asthma deaths, though the numbers in the study were small and the interpretation is still a matter of controversy.

LABAs should be used prudently:

- always use in combination with other appropriate asthma control medications (e.g., inhaled corticosteroids), never as mono therapy of asthma;
- combine with a medium dose ICS before using high dose ICS (see ICS, above);
- use on a scheduled basis, not for management of worsening asthma;
- **not for exacerbations.**

Patients should be cautioned not to discontinue their established LABA without consulting their health care provider.

Leukotriene receptor antagonists (LTRA) can be useful in controlling asthma in infants, children, and adults.

Current data suggests that monotherapy with leukotriene modifier agents is more likely to be successful for prophylaxis in mild persistent asthma and exercise-induced bronchospasm, especially when allergic rhinitis is a comorbid condition. Leukotriene modifiers have not been studied as monotherapy for severe persistent asthma. Leukotriene modifiers have been used as adjuvants to inhaled corticosteroids in severe persistent asthma, though not studied extensively for this purpose. Numerous studies have shown leukotriene modifiers to be less effective than long-acting β_2 -agonists (LABAs) when added to inhaled corticosteroids as the second-line agent.

Three leukotriene modifier agents approved by the FDA are currently available for the treatment of chronic asthma. Zafirlukast (Accolate) and montelukast (Singulair) are leukotriene receptor antagonists and zileuton (Zyflo) is a 5-lipoxygenase inhibitor. These agents have been shown clinically to inhibit exercise-induced bronchoconstriction as well as reduce daytime symptom scores, nighttime asthma, rescue β -agonist use and improve PEFr and FEV1 in chronic asthma. In a controlled study comparing these agents to inhaled corticosteroids, beclomethasone 200 mg bid outperformed montelukast 10 mg daily. A second 14-week controlled cross over study in 192 subjects with moderate asthma examined the time to treatment failure comparing (a) regular treatment with the LABA salmeterol in combination with montelukast to (b) beclomethasone and salmeterol. The combination of montelukast and salmeterol was significantly inferior to salmeterol and beclomethasone ($p=0.0008$) and the study was discontinued after 12 weeks by the study's Drug and Safety Monitoring Board.

Montelukast can be administered without regard to food, while zafirlukast must be dosed one hour before or 2 hours after eating. Zafirlukast is approved for ages >5 years and montelukast is approved for ages >6 months using the oral granules. Zafirlukast can potentiate warfarin and theophylline as well as interact with several other medications. Drug interactions with montelukast are rare. Post marketing surveillance of adverse effects reported with montelukast has been recently updated to include psychomotor hyperactivity (including irritability, agitation, aggressive behavior, restlessness, and tremor), and seizures. With regard to LTRAs, the FDA states that "healthcare professionals should consider discontinuing these medications if patients develop neuropsychiatric symptoms." Churg-Strauss vasculitis has rarely been reported in association with montelukast or zafirlukast in patients tapering chronic systemic corticosteroids. The FDA mandates monitoring hepatic enzymes with zileuton.

Mast cell stabilizers, i.e. cromolyn sodium and nedocromil, are non-steroidal drugs with anti-inflammatory properties that can be used to control symptoms in patients with mild persistent asthma.

Their mechanism of action in vivo remains unknown though it has been attributed to stabilization of mast cells and prevention of mediator release. Though these drugs are traditionally thought to have a special role in the treatment of exercise- and allergen-induced bronchospasm, there is in fact no way to predict reliably which patients will respond to them. Cromolyn has no special advantage over prophylactic use of β_2 -agonists or inhaled corticosteroids for maintenance therapy when these other medications are effective and well tolerated. Recent randomized controlled trials in children and observational data in adults do not demonstrate cromolyn or nedocromil to be superior to placebo for non-exercise-induced asthma. Some experts believe there is a subset (perhaps 5-10%) of adult asthmatics who derive additional benefit to that obtained from maximal tolerated doses of inhaled corticosteroids, β_2 -agonists, and methylxanthines. While there may be situations where

cromolyn sodium or nedocromil may be useful, they should in general be considered second or third line agents.

Methylxanthines could be used to control symptoms in older children and adults with mild persistent asthma.

They exhibit only mild to moderate bronchodilator activity but have additional effects that may be beneficial in the management of asthma. Methylxanthines are quite useful for managing patients with variable or nocturnal symptoms not readily controlled with inhaled medication (anti-inflammatory and β_2 -agonist). Theophylline bronchodilator response is roughly linear with serum concentration. Traditionally, levels of 10-20 mcg/mL have been suggested as an optimal compromise between safety and efficacy. Recent data suggest that side-effects are minimized and safety more easily maintained with levels between 5-15 mcg/mL. Potential drug interactions and clearance-altering co-morbidities (heart and liver disease, smoking, erythromycin, cimetidine and others) must be carefully screened with dosage adjustments as indicated. Current practice tends to use theophylline as an adjunct to inhaled corticosteroid therapy, not as the mainstay. Sustained release theophylline is a convenient way to maintain steady-state levels in the therapeutic range. Sustained release products should be chosen on the basis of cost. Scientific evidence does not support or reject use of theophylline in severe acute asthma.

Systemic (oral) corticosteroids are used to treat exacerbations and as maintenance therapy in steroid-dependent severe persistent asthma.

Systemic corticosteroids have numerous significant and undesirable long term side effects for both adults and children. Therefore their long term use is undesirable and only recommended in the most severe cases. Patients in this category should be referred for specialist/subspecialist evaluation.

In asthma, the mechanism of action of corticosteroids is not entirely established but includes: interference with arachidonic acid metabolism and the synthesis of leukotrienes; prevention of the directed migration and activation of inflammatory cells; and increased responsiveness of β_2 -receptors of the airway smooth muscle. No consensus exists on the specific type, dose, or duration of corticosteroid to be used in the treatment of asthma. Systemic corticosteroid bursts with or without a taper are generally used for acute exacerbations. If chronic long-term therapy is required, alternate day administration of oral corticosteroids is preferable to daily treatment. In most cases, it is strongly recommended that inhaled corticosteroids be added to the regimen when oral corticosteroids are started to reduce or eliminate chronic long-term oral therapy. Use of systemic corticosteroids within 1 hour of presentation of adults and children with acute asthma to the emergency department has been shown to significantly reduce hospital admission. Benefits were greatest in patients with more severe asthma and those not currently receiving systemic steroids.

Chronic systemic corticosteroid therapy may be associated with obesity, moon facies, supraclavicular and nuchal fat pads, striae, easy bruisability, weakness, hypertension, osteopenia, and glucose intolerance. Children may also exhibit growth failure. Long-term (>2 weeks) corticosteroid therapy may cause suppression of the hypothalamic-pituitary-adrenal axis. Full recovery of the axis can take up to 12 months depending on the dose, frequency, and duration of antecedent therapy. Symptoms and signs of secondary adrenal insufficiency include weakness, weight loss, and gastrointestinal discomfort. Adrenal insufficiency can evolve into acute adrenal crisis precipitated by severe infection, trauma, or surgery. Clinical presentation includes fever, dehydration, hypotension, nausea, vomiting, and hypoglycemia. Patients with asthma in general and especially those using inhaled or systemic corticosteroids should have their asthma in good control prior to surgery and may require a pre-operative stress-dose or pharmacologic dose of a systemic corticosteroid to minimize morbidity secondary to inflammation, bronchoconstriction and potential adrenal insufficiency associated with endotracheal intubation. Systemic corticosteroid therapy can cause osteopenia and osteoporosis.

Pediatric considerations. In managing pediatric patients, few recommendations guide the clinician and fewer criteria exist on which to base fundamental treatment decisions. The FDA has not approved the use of many effective anti-asthma drugs in the very young. However, in the absence of needed studies, "lack of approval" does not constitute "disapproval."

Metered dose inhalers (MDIs) must be used in infants and children with appropriate spacer devices (VHC) with either a mask or mouth piece. Infants and smaller children need MDI doses equivalent to adult doses because they inhale aerosols during tidal breathing without a breath hold, thus decreasing retention time and effective drug delivery to the lungs. Compressed air-driven, wet nebulizers are commonly available for home administration of β_2 -agonists, cromolyn sodium, ipratropium bromide, and the corticosteroid budesonide. Complete nebulization of medication is time consuming, and the infant or young child must keep the mask in place for the duration of therapy. Older children may use a mouthpiece instead. Using a face mask made for delivering the medication is important. Attempting to short-cut the process by partially blocking one side of the nebulizer mouth piece and using the nebulizer machine to blow the medicine at the face/nose (i.e. "blow by") is ineffective and must be avoided. Pediatric patients may be uncooperative with nebulized medication delivery. If proper administration is not tolerated by the child, a metered-dose inhaler with spacer and mask should be used instead.

Administration of inhaled medication via MDIs, Nebulizers and DPIs requires deliberate patient and family education and their understanding of technique. A guide for the proper

use of these devices and to figure out the VHC size is available at

www.med.umich.edu/1info/fhp/practiceguides/asthma.html

Home nebulizers have been shown to be no more effective than MDIs in the management of asthma, and may be less effective than MDIs with valved holding chambers (VHC). They may be helpful in the minority of patients who cannot use a metered dose inhaler and VHC properly. Patients and care-givers need instruction in the mechanical use of the nebulizer; this should be done by a clinician or respiratory therapist. Patients and care-givers must also be instructed in frequency dose and monitoring parameters for nebulized medications.

Treating related comorbidities. Some drugs may be useful for asthma patients with related comorbid conditions.

COPD and anticholinergics. Anticholinergics are useful in COPD and in status asthmaticus. The benefits of daily use for asthma in children and adults have not been established, even though they are commonly used for refractory patients.

Allergic asthma and omalizumab. This agent is recommended only for use in patients age 12 years and older with severe persistent asthma allergic under a specialist's care for management. This recombinant anti-IgE antibody can be administered subcutaneously monthly or biweekly. It improves control for severe allergic asthma patients who are using maximal doses of conventional therapy. Clinicians must be prepared to treat potential anaphylactic reactions and monitor patients for a minimum of 2 hours following each dose.

Anti-reflux therapy. Treating gastroesophageal reflux disease (GERD) can reduce airway hyper-responsiveness and improve pulmonary function for patients with asthma and GERD.

Peak Expiratory Flow Rate (PEFR) Monitoring

PEFR is a simple quantitative method for

- Assessing level of control
- Assessing diurnal variation
- Identifying triggers

A recent meta-analysis provided evidence that symptom-based monitoring may be slightly superior to peak flow monitoring for patients in general. PEFR based monitoring may be useful for patients who have difficulty perceiving signs of worsening asthma. PEFR monitoring provides objective information that can be used *by adults and children as young as 5 years old* though readings may be less consistent in children under age 8.

Clinicians may consider home peak flow monitoring in patients *over 5 years of age* who have:

- (1) poor perception of the severity of their asthma (poor perception = clinical assessment does not match patient's awareness of severity)

- (2) wide fluctuations in level of control

In managing *mild or intermittent asthma*, long-term daily peak flow measurement does *not* appear to affect outcomes significantly.

Use of the peak flow monitor requires *deliberate patient education and patient understanding of technique*. Once the technique is learned, the patient is normally encouraged to make three attempts and record the best of the three when taking readings.

Personal best PEFR. This value is the standard for assessing control. The value is determined by measuring peak flow twice daily over a 2-3 week period. "Personal best" is the highest value during a period of maximal therapy. If the patient uses a bronchodilator, a PEFR should be measured before and after using the bronchodilator. It is best if all measured values are recorded in a log book, diary, or chart with dates and times and brought to visits when control and severity are being determined. An example of a peak flow record chart is available at www.med.umich.edu/1info/fhp/practiceguides/.

In children, the personal best value should be re-evaluated yearly to account for growth. The most useful standard for ongoing monitoring is the patient's personal best PEFR. As a general reference, nomograms of normal predicted average peak expiratory flow values for children, adolescents, and adults are available at www.med.umich.edu/1info/fhp/practiceguides/asthma.html

Spirometry. Spirometry can be reliably performed by adults and children over age 5 years. It is the only functional test that should be used for diagnosing asthma. It is also used for monitoring response to therapy. It should be considered if there is doubt in the reliability of peak flow monitoring.

Asthma Action Plan

An asthma action plan (AAP) developed for the patient functions as a summary of teaching for management and a quick reference for managing an exacerbation. Zones are defined for "doing well," "caution," and "medical alert." Asthma is self-managed using controller medications (if persistent asthma) and by monitoring symptoms and PEFR to guide use of rescue medications and emergency treatment. Models for AAPs are presented in the Appendix, with separate models for ages 0–4 years, 5–11 years, and 12 years and older. Copies of the models that can be edited and downloaded for printing are available at www.med.umich.edu/1info/fhp/practiceguides/asthma.html.

Provide a written AAP to all patients with persistent asthma. An AAP is often useful for patients with intermittent asthma. Explain the three zones and the self-management steps the patient is to take (see below), writing the management instructions on the AAP for this patient. A written copy of the plan should be placed in the patient record and a copy provided to the patient/family to use at home.

Green, yellow, and red zones. Define and explain to the patient the three zones: green = doing well, yellow = caution, and red = medical alert. These zones are explained in more detail below.

Green Zone (no symptoms, 80-100% of personal best PEFR). No coughing, wheezing, chest tightness, or shortness of breath during the day or night, able to do all usual activities = “all clear”

Controller medications (such as inhaled steroids) with specific use instructions should be written in the green zone. Individuals with exercise-induced bronchospasm may have a rescue inhaler (SABA) included in the green zone, but these medications should otherwise be in the yellow zone under rescue medications.

Yellow Zone (some symptoms, 50-80% of personal best PEFR). Has breathing problems, can do some, but not all usual activities, sleep disturbance = “caution” indicating suboptimal control or early exacerbation. SABA specifics should be listed here. Encourage continued administration of all the controller medications listed in the green zone. There should also be specific instructions about seeking help if the patient’s symptoms are not returning to the green zone.

Red Zone (severe symptoms, <50% of personal best PEFR). Breathing is hard and fast, respiratory distress is evident (nasal flaring, chest retractions) = “alert” indicating need for initiation of more intense treatment. Patients should seek medical help immediately, either calling their doctor or for emergency help, and then possibly use more SABA. Oral corticosteroids may be included in the red or yellow zone in selected patients, particularly more severe and pediatric patients.

Prevention

Patients with asthma should receive all routine preventive care and vaccinations recommended for otherwise healthy adults. Additionally, patients with asthma are at increased risk for complications from pulmonary infections (e.g., hospitalization, increased use of antibiotics). Therefore the CDC Advisory Committee of Immunization Practices recommends all patients older than 6 months receive influenza vaccine and that all adults receive pneumococcal polysaccharide vaccine.

Influenza vaccination is performed annually for all patients with asthma over 6 months of age. Vaccination is typically performed in the fall to maximize resistance during the winter “flu season.” Children under 9 years of age receiving influenza vaccine for the first time, should receive a booster dose 1 month after the first injection. Children who only receive 1 of the 2 recommended doses in their first year vaccination should receive 2 doses the second year. Influenza vaccination has not been shown to reduce the frequency or severity of asthma exacerbations during the influenza season, and patients should not have this expectation.

Pneumococcal polysaccharide vaccination is generally recommended for patients with asthma, with some current variation in the phrasing of recommendations by age group. This vaccination is recommended for all children (with or without asthma) younger than 6 years. Administer 1 dose to all healthy children age 24 to 59 months. This vaccination is recommended for children and adolescents age 7 - 17 years who have severe asthma and require chronic high dose oral corticosteroids. This vaccination is recommended for all adults with asthma. If the initial dose is given at an age < 65 years old, a second dose should be administered when the individual is ≥ 65 years old and ≥ 5 years have passed since the initial vaccination.

Follow up

For patients whose treatment for asthma has just been initiated, a follow-up assessment should occur in 2 to 6 weeks. In determining the time frame within this range for a specific patient, consider the severity of the conditions and the potency of the initial intervention.

Ongoing Asthma Management

Ongoing management control is summarized in the last section of Table 1 and explained in more detail below.

Assess Asthma Control

Assess control to monitor and adjust therapy. Patients are typically classified as “well controlled,” “not well controlled,” or “very poorly controlled.” The factors used to assess control are almost identical to those used for initial classification. The values that indicate level of control are presented in Table 9. Note that acceptable values vary by age.

Assessing control is done with symptom monitoring, peak flow monitoring, and spirometry. Peak flow monitoring may be more useful than symptom base monitoring in patients who are “poor perceivers”.

A recent meta-analysis provided evidence that symptom-based monitoring may be slightly superior to peak flow monitoring for patients in general. Spirometry is recommended at the time of initial assessment, after treatment is initiated and symptoms and PEF have stabilized, during periods of progressive or prolonged loss of asthma control, and at least every 1–2 years.

Environmental Control

Follow-up on the patient’s understanding and identification of triggers. Find out steps taken to avoid triggers and success in avoidance. Address tobacco smoke exposure (smoking and passive smoke). As appropriate, advise regarding improving environmental control.

Medical Therapy

The level of asthma control directs maintaining or adjusting medical therapy. The bottom of Table 9 shows the action by level of control, with well controlled patients maintaining current therapy, not well controlled patients stepping up 1 level of therapy, and very poorly controlled patients stepping up 1-2 steps with consideration of a short course of oral corticosteroids. Table 7 defines the treatment at each step.

Increasing/frequent use of SABAs for “rescue” from exacerbations generally indicates inadequate control and the need to step up treatment. For all ages consideration should be given to stepping up treatment when a patient uses SABAs more than 2 days/week for symptoms (not exercise-induced)

On subsequent follow up visits, if a patient remains well controlled for 3 months or longer, consider reducing treatment by one step.

Review Proper Technique or the Administration of Inhaled Medications.

Optimal delivery of inhaled medications via MDIs with Valved Holding Chamber, Nebulizers or DPIs depends greatly on the way the specific delivery system is used. Patient and care givers understanding and mastering of the proper technique should be reviewed on a regular basis, e.g., [Instructions for various MDI delivery devices](#)

Review/Revise Asthma Action Plan

Review patient’s understanding of and adherence to the current Asthma Action Plan. The review includes asthma self-management using controller and rescue medications when in the green, yellow, and red zones. The Asthma Action Plan should be reviewed every time the therapeutic regimen changes. If no changes are made, the Asthma Action Plan should be re-written annually.

If the patient’s level of asthma control needs no change in medical therapy, reinforce use of the current plan.

If the level of asthma control indicates a step down or step up in recommended medical therapy, explain the change in management and write out a new Asthma Action Plan. A written copy of the new plan should be placed in the patient record and a copy provided to the patient/family to use at home.

Prevention at Follow-up

Review the status of vaccinations for influenza and for pneumococcal disease to be sure they have been administered.

Plan ahead for the annual influenza vaccination. If the patient does not have a visit scheduled for the fall, special

notification may be sent in the fall to remind the patient to get an annual flu vaccination.

When patients become age 65 years, review the date at which the pneumococcal vaccination occurred. Determine whether and when a second vaccination is needed. For individuals age ≥ 65 years who were vaccinated at age < 65 years, a second vaccination should be given ≥ 5 years after the initial vaccination.

Referral to Asthma specialist

Refer to a specialist when:

- Diagnosis is in doubt. Signs and symptoms are atypical, or there are problems in differential diagnosis.
- Inadequate response to asthma treatment, especially if multiple courses of oral steroids, emergency or hospital treatment required.
- Patient requires step 4 care or higher (step 3 for children 0–4 years of age). Consider referral if patient requires step 3 care (step 2 for children 0–4 years of age).
- Multiple confounding diagnoses.
- Suspected allergy requiring allergen testing and consideration of immunotherapy.
- Occupational asthma
- Problems with adherence requiring a multidisciplinary team approach (including additional education efforts).
- Psychosocial problems or disability interfering with adherence/treatment.

Follow-Up

Optimal intervals for follow up have not been specifically studied. Current recommendations are:

- 2-6 weeks on initiation, significant change in status, or step-up in treatment
- 3 months after step-down in treatment
- 3-6 months with stable control and symptoms

Special Circumstances

Pregnancy and Breast Feeding

Asthma is generally managed the same for pregnant and non-pregnant women. Better pregnancy outcomes have been seen with good control, specifically reduced risk of mild prematurity, pre-eclampsia, and growth restriction. Systematic reviews of evidence show that long and short acting beta-agonists, cromolyn, and inhaled corticosteroids are safe in pregnancy. Inhaled corticosteroids reduce the risk of pregnancy-associated exacerbations. The bulk of the data on inhaled corticosteroids is with budesonide; other agents have not been well studied. Systemic corticosteroid use in the first trimester is associated with cleft lip and palate, and later in pregnancy with pregnancy-induced hypertension and possibly preeclampsia. Theophylline in high doses is associated with adverse pregnancy outcomes;

while usual doses are safe, unacceptable side effects are frequent. Few data are available about antileukotrienes in pregnancy. A recent trial suggests a slightly higher rate of major structural defects.

Breast feeding by women with asthma is generally managed in the same manner as for other women who are breast feeding. All commonly used asthma agents except Zafirlukast are considered “probably compatible” with breastfeeding. This is based on extremely limited data, with most drugs having only information about low amounts excreted in breast milk (some have no data at all), and no reports of any problems. Zafirlukast’s manufacturer has recommended against its use in breastfeeding because of reports of tumors in mice. Prednisone alone has been shown to be present in negligible amounts in breast milk, and is rated as “compatible”. Montelukast is present in significant amounts in breast milk.

Surgery

For elective surgical patients with asthma, the goal is for the asthma to be well controlled through optimal therapy. This is accomplished by the usual classification of asthma severity and control, with stepped therapy when needed (see Tables 6 & 7). If the patient’s asthma is well controlled, no further intervention is necessary. Stress-dose steroids may be required for patients on chronic oral steroids.

Complimentary/Alternative Treatment

Non-traditional treatments, including manual therapy, acupuncture, and Chinese herbal medicine, have not shown significant beneficial effects.

Literature Search and Recommendations

The team began the search of literature by accepting the results of the literature search performed for the National Asthma Education and Prevention Program Expert Panel Report 3: Guidelines for the Diagnosis and management of Asthma, July 2007. That group systematically reviewed evidence published through March 15, 2006.

To update that search with more recent literature, a systematic search of literature on Medline was performed for the period from 1/1/06 through 1/30/08. The major search term was asthma and the search was performed for literature on humans (adult and pediatric) in the English language. Searches were performed on the following specific topics.

- Diagnosis and: history (rhinitis, nasal polyps, atopic dermatitis); physical exam, signs, symptoms (normal, wheezing, intercostal retraction during inspiration, chest hyperinflation, prolonged expiratory phase); spirometry; and other references to diagnosis.

- Treatment and: disease management programs; self management (including action plan and patient education); objective assessment (peak expiratory flow rate [PEFR] monitoring); avoid, control triggers (smoking, allergens, foods, indoor air pollution, medications, exercise, concurrent medical conditions, environmental control); pharmacotherapy; adverse effects of pharmacotherapy; complementary alternative, and integrative medicine; follow up, consultation, referral; pregnancy, other references to treatment or management.
- Other references not associated with diagnosis or treatment.

The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was supplemented with very recent clinical trials known to expert members of the panel. Negative trials were specifically sought. The search was a single cycle.

Conclusions were based on prospective randomized clinical trials if available, to the exclusion of other data; if RCTs were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size. The “strength of recommendation” for key aspects of care was determined by expert opinion.

Related National Guidelines

This guideline is consistent with the National Asthma Education and Prevention Program Expert Panel Report 3: Guidelines for the Diagnosis and management of Asthma (2007).

Disclosures

The University of Michigan Health System endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is made to provide readers with information that might be of potential importance to their evaluation of the information.

Team Member	Relationship	Company
Manuel Arteta, MD	None	
Alan P Baptist, MD	None	
James A Freer, MD	None	
Cyril M Grum MD	None	
R Van Harrison, PhD	None	
Cary E Johnson, PharmD	None	
Joyce E Kaferle, MD	None	
Sean K Kesterson, MD	None	
Jill A Noble, MD	None	

Lung, and Blood Institute, 2007. (Publication No. 08-4051; available at: www.nhlbi.nih.gov/guidelines/asthma/)

This full report (440 pages) presents their guidelines along with the detailed methodology underlying their development. A shorter (74 page) summary of the guidelines is also available at the same web site (Publication No. 08-5846).

Working Group Report on Managing Asthma During Pregnancy: Recommendations for Pharmacologic treatment – Update 2004, NIH publication No. 05-5236. Bethesda, MD: National Heart, Lung, and Blood Institute, 2005.

This resource addresses asthma and pregnancy.

Acknowledgements

The following individuals are acknowledged for their contributions to previous versions of this guideline.

1996: Cyril M. Grum, MD, James L. Baldwin, MD, Ann M Durnace, RN, Steven R. Erickson, PharmD, Lee A. Green, MD, MPH, Martin E. Hurwitz, MD, Sonya Mitrovich, MD, John G. Younger, MD

2000 (and revised 2004): Lee A. Green, MD, MPH, James L. Baldwin, MD, Steven R. Erickson, PharmD, Cyril M. Grum, MD, Martin E. Hurwitz, MD, Sonya Mitrovich, MD, John G. Younger, MD

2005 (and revised 2006): Lee A. Green, MD, MPH, James L. Baldwin, MD, F. John Brinley, MD, James A. Freer, MD, Cyril M. Grum, MD, Martin E. Hurwitz, MD, Cary E. Johnson, PharmD, Benjamin Song, MD

2009: Annie Sy, PharmD, helped adapt NHLBI guidelines into Table 6 (initial classification) and Table 9 (follow-up classification)

Review and Endorsement

Drafts of this guideline were reviewed in clinical conferences and by distribution for comment within departments and divisions of the University of Michigan Medical School to which the content is most relevant: Allergy, Emergency Medicine, Family Medicine, General Medicine, General Pediatrics, Geriatric Medicine, Obstetrics & Gynecology (Women’s Health), Pediatric Pulmonology, and Pulmonary & Critical Care Medicine. The Executive Committee for Clinical Affairs of the University of Michigan Hospitals and Health Centers endorsed the final version.

Annotated References

National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Bethesda, MD: National Heart,

APPENDIX

Asthma Action Plan Models for:

- 1. Ages 0–4 Years**
- 2. Ages 5–11 Years**
- 3. Ages \geq 12 Years**

Copies of the individual models that can be edited and downloaded for printing are available at www.med.umich.edu/info/fhp/practiceguides/.

For University of Michigan Healthcare Providers, asthma action plans may be accessed through the Health Maintenance/Chronic Care Management section of the Problem Summary List of CareWeb and completed on-line.

University of Michigan Hospitals & Health Centers
Asthma Action Plan for Patients 0 – 4 Years

Name: _____	
Reg #:	Date: _____
DOB:	Age: _____

<p>GREEN ZONE (Doing Well)</p> <p>✓ Breathing is good (no coughing, wheezing, chest tightness, or shortness of breath during the day or night), and</p> <p>✓ Able to do usual activities (work, play, and exercise)</p>	<p>Controller Medications</p> <p>Give these medication(s) to your child EVERY DAY.</p> <table border="1"> <thead> <tr> <th style="width: 50%;">Medication</th> <th style="width: 50%;">Directions</th> </tr> </thead> <tbody> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> </tbody> </table>	Medication	Directions														
Medication	Directions																
<p>YELLOW ZONE (Caution)</p> <p>✓ Breathing problems (coughing, wheezing, chest tightness, shortness of breath, or waking up from sleep), or</p> <p>✓ Can do some, but not all, usual activities</p> <p><i>Call your doctor if you are not sure whether your child's symptoms are due to asthma.</i></p>	<p>Rescue Medications</p> <p>Continue giving the controller medication(s) as prescribed.</p> <p>Give: _____</p> <p>Then: • Wait 20 minutes and see if the treatment(s) helped</p> <p>• If your child is GETTING WORSE or is NOT IMPROVING after the treatment(s), go to the Red Zone</p> <p>• If your child is BETTER, _____</p> <p>Then: If your child still has symptoms after 24 hours, CALL YOUR CHILD'S DOCTOR and if he/she agrees:</p> <p><input type="checkbox"/> Start: _____</p> <p><input type="checkbox"/> Other: _____</p> <p><i>If rescue medication is needed more than 2 times a week, call your child's doctor at _____.</i></p>																
<p>RED ZONE (Medical Alert)</p> <p>✓ Breathing is hard and fast (nose opens wide, ribs show), or</p> <p>✓ Quick-relief medications have not helped, or</p> <p>✓ Cannot do usual activities (including trouble talking or walking)</p>	<p>Emergency Treatment</p> <p>Give these medication(s) AND seek medical help NOW.</p> <p>Take: _____</p> <p>Then: • Wait 15 minutes and see if the treatment(s) helped</p> <p>• If your child is GETTING WORSE or is NOT IMPROVING, go to the hospital or call 9-1-1</p> <p>• If your child is BETTER, continue treatments every 4 to 6 hours and call your child's doctor – say your child is having an asthma attack and needs to be seen TODAY</p> <p>Then: <input type="checkbox"/> If your doctor agrees, start: _____</p> <p><input type="checkbox"/> Other: _____</p>																

Plan Developed in Partnership with Patient's Family by (Doctor's Name): _____ Doctor Number: _____
 Signature: _____ Date/Time: _____


POD-0241	REV: 12/09 HIM: 12/09	Medical Records		Asthma Action Plan Patients 0 – 4 Years
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University of Michigan Hospitals & Health Centers
Asthma Action Plan for Patients 5 – 11 Years

Name: _____	
Reg #:	Date: _____
DOB:	Age: _____

<p>GREEN ZONE (Doing Well)</p> <p>✓ Breathing is good (no coughing, wheezing, chest tightness, or shortness of breath during the day or night), and</p> <p>✓ Able to do usual activities (work, play, and exercise), and</p> <p>✓ Peak flow is more than 80% of your child's personal best (_____)</p> <p>Personal Best: _____</p>	<p>Controller Medications</p> <p>Take these medication(s) EVERY DAY.</p> <table border="1" style="width: 100%;"> <thead> <tr> <th style="width: 50%;">Medication</th> <th style="width: 50%;">Directions</th> </tr> </thead> <tbody> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> </tbody> </table> <p><input type="checkbox"/> If your child usually has symptoms with exercise, then give: _____</p>	Medication	Directions																
Medication	Directions																		
<p>YELLOW ZONE (Caution)</p> <p>✓ Breathing problems (coughing, wheezing, chest tightness, shortness of breath, or waking up from sleep), or</p> <p>✓ Can do some, but not all, usual activities, or</p> <p>✓ Peak flow is between 60% to 80% of your child's personal best (_____ to _____)</p>	<p>Rescue Medications</p> <p>Continue giving the controller medication(s) as prescribed.</p> <p>Give: _____</p> <p>Then: • Wait 20 minutes and see if the treatment(s) helped</p> <p>• If your child is GETTING WORSE or is NOT IMPROVING after the treatment(s), go to the Red Zone</p> <p>• If your child is BETTER, _____</p> <p>Then: If your child still has symptoms after 24 hours, CALL YOUR CHILD'S DOCTOR and if he/she agrees:</p> <p><input type="checkbox"/> Start: _____</p> <p><input type="checkbox"/> Other: _____</p> <p>If rescue medication is needed more than 2 times a week, call your child's doctor at _____.</p>																		
<p>RED ZONE (Medical Alert)</p> <p>✓ Breathing is hard and fast (nose opens wide, ribs show), or</p> <p>✓ Rescue medications have not helped, or</p> <p>✓ Cannot do usual activities (including trouble talking or walking), or</p> <p>✓ Peak flow is less than 60% of your child's personal best (_____)</p>	<p>Emergency Treatment</p> <p>Take these medication(s) and seek medical help NOW.</p> <p>Take: _____</p> <p>Then: • Wait 15 minutes and see if the treatment(s) helped</p> <p>• If your child is GETTING WORSE or is NOT IMPROVING, go to the hospital or call 9-1-1</p> <p>• If your child is BETTER, continue treatments every 4 to 6 hours and call your child's doctor – say your child is having an asthma attack and needs to be seen TODAY</p> <p>Then: <input type="checkbox"/> If your doctor agrees, start: _____</p> <p><input type="checkbox"/> Other: _____</p>																		

Plan Developed in Partnership with Patient's Family by (Doctor's Name): _____ Doctor Number: _____
 Signature: _____ Date/Time: _____

POD-0242	REV: 12/09 HIM: 12/09	Medical Records		Asthma Action Plan Patients 5 – 11 Years
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University of Michigan Hospitals & Health Centers
Asthma Action Plan for Patients 12 Years or Older

Name: _____	
Reg #:	Date: _____
DOB:	Age: _____

<p>GREEN ZONE (Doing Well)</p> <ul style="list-style-type: none"> ✓ Breathing is good (no coughing, wheezing, chest tightness, or shortness of breath during the day or night), and ✓ Able to do usual activities (work, play, and exercise), and ✓ Peak flow is more than 80% of your personal best (_____) <p>Personal Best: _____</p>	<p>Controller Medications Take these medication(s) EVERY DAY.</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 50%;">Medication</th> <th style="width: 50%;">Directions</th> </tr> </thead> <tbody> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> <tr><td> </td><td> </td></tr> </tbody> </table> <p><input type="checkbox"/> If you usually have symptoms with exercise, then take: _____</p>	Medication	Directions																				
Medication	Directions																						
<p>YELLOW ZONE (Caution)</p> <ul style="list-style-type: none"> ✓ Breathing problems (coughing, wheezing, chest tightness, shortness of breath, or waking up from sleep), or ✓ Can do some, but not all, usual activities, or ✓ Peak flow is between 60% to 80% of your personal best (_____ to _____) 	<p>Rescue Medications Continue taking your controller medication(s) as prescribed.</p> <p>Take: _____</p> <p>Then: • Wait 20 minutes and see if the treatment(s) helped</p> <ul style="list-style-type: none"> • If you are GETTING WORSE or are NOT IMPROVING after the treatment(s), go to the Red Zone • If you are BETTER, _____ <p>Then: If you still have symptoms after 24 hours, CALL YOUR DOCTOR and if he/she agrees:</p> <p><input type="checkbox"/> Start: _____</p> <p><input type="checkbox"/> Other: _____</p> <p><i>If rescue medication is needed more than 2 times a week, call your doctor at _____.</i></p>																						
<p>RED ZONE (Medical Alert)</p> <ul style="list-style-type: none"> ✓ Breathing is hard and fast (nose opens wide, ribs show), or ✓ Rescue medications have not helped, or ✓ Cannot do usual activities (including trouble talking or walking), or ✓ Peak flow is less than 60% of your personal best (_____) 	<p>Emergency Treatment Take these medication(s) and seek medical help NOW.</p> <p>Take: _____</p> <p>Then: • Wait 15 minutes and see if the treatment(s) helped</p> <ul style="list-style-type: none"> • If you are GETTING WORSE or are NOT IMPROVING, go to the hospital or call 9-1-1 • If you are BETTER, continue treatments every 4 to 6 hours and call your doctor – say you are having an asthma attack and need to be seen TODAY <p>Then: <input type="checkbox"/> If your doctor agrees, start: _____</p> <p><input type="checkbox"/> Other: _____</p>																						

Plan Developed in Partnership with Patient by (Doctor's Name): _____ Doctor Number: _____
 Signature: _____ Date/Time: _____

POD-0243	REV: 12/09 HIM: 12/09	Medical Records	 <small>University of Michigan</small>	<small>Asthma Action Plan Patients 12 Years or Older</small>
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