

FIGURE 3-4a. STEPWISE APPROACH FOR MANAGING ASTHMA IN ADULTS AND CHILDREN OLDER THAN 5 YEARS OF AGE

Goals of Asthma Treatment

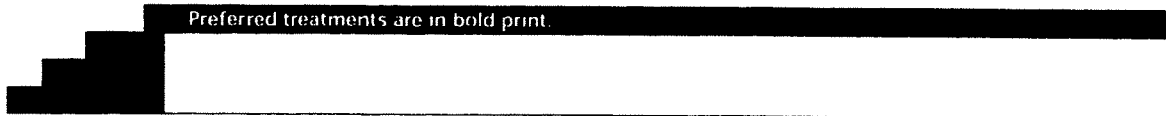
- Prevent chronic and troublesome symptoms (e.g., coughing or breathlessness in the night, in the early morning, or after exertion)
- Maintain (near) "normal" pulmonary function
- Maintain normal activity levels (including exercise and other physical activity)
- Prevent recurrent exacerbations of asthma and minimize the need for emergency department visits or hospitalizations
- Provide optimal pharmacotherapy with minimal or no adverse effects
- Meet patients' and families' expectations of and satisfaction with asthma care

Classify Severity of Asthma			
Clinical Features Before Treatment*			
	Symptoms**	Nighttime Symptoms	Lung Function
STEP 4 Severe Persistent	<ul style="list-style-type: none"> ■ Continual symptoms ■ Limited physical activity ■ Frequent exacerbations 	Frequent	<ul style="list-style-type: none"> ■ FEV₁ or PEF ≤ 60% predicted ■ PEF variability > 30%
STEP 3 Moderate Persistent	<ul style="list-style-type: none"> ■ Daily symptoms ■ Daily use of Inhaled short-acting beta₂-agonist ■ Exacerbations affect activity ■ Exacerbations ≥ 2 times a week; may last days 	> 1 time a week	<ul style="list-style-type: none"> ■ FEV₁ or PEF > 60% – < 80% predicted ■ PEF variability > 30%
STEP 2 Mild Persistent	<ul style="list-style-type: none"> ■ Symptoms > 2 times a week but < 1 time a day ■ Exacerbations may affect activity 	> 2 times a month	<ul style="list-style-type: none"> ■ FEV₁ or PEF ≥ 80% predicted ■ PEF variability 20–30%
STEP 1 Mild Intermittent	<ul style="list-style-type: none"> ■ Symptoms ≤ 2 times a week ■ Asymptomatic and normal PEF between exacerbations ■ Exacerbations brief (from a few hours to a few days); intensity may vary 	≤ 2 times a month	<ul style="list-style-type: none"> ■ FEV₁ or PEF ≥ 80% predicted ■ PEF variability < 20%

* The presence of one of the features of severity is sufficient to place a patient in that category. An individual should be assigned to the most severe grade in which any feature occurs. The characteristics noted in this figure are general and may overlap because asthma is highly variable. Furthermore, an individual's classification may change over time.

** Patients at any level of severity can have mild, moderate, or severe exacerbations. Some patients with intermittent asthma experience severe and life-threatening exacerbations separated by long periods of normal lung function and no symptoms.

FIGURE 3-4b. STEPWISE APPROACH FOR MANAGING ASTHMA IN ADULTS AND CHILDREN OLDER THAN 5 YEARS OF AGE: TREATMENT (CONTINUED)



	Long-Term Control	Quick Relief	Education
STEP 2 Mild Persistent	<p>One daily medication:</p> <ul style="list-style-type: none"> ■ Anti-inflammatory: either inhaled corticosteroid (low doses) or cromolyn or nedocromil (children usually begin with a trial of cromolyn or nedocromil). ■ Sustained-release theophylline to serum concentration of 5-15 mcg/mL is an alternative, but not preferred, therapy. Zafirlukast or zileuton may also be considered for patients >12 years of age, although their position in therapy is not fully established. 	<ul style="list-style-type: none"> ■ Short-acting bronchodilator: inhaled beta₂-agonists as needed for symptoms. ■ Intensity of treatment will depend on severity of exacerbation; see component 3-Managing Exacerbations. ■ Use of short-acting inhaled beta₂-agonists on a daily basis, or increasing use, indicates the need for additional long-term-control therapy. 	<p>Step 1 actions plus:</p> <ul style="list-style-type: none"> ■ Teach self-monitoring ■ Refer to group education if available ■ Review and update self-management plan
STEP 1 Mild Intermittent	<ul style="list-style-type: none"> ■ No daily medication needed. 	<ul style="list-style-type: none"> ■ Short-acting bronchodilator: inhaled beta₂-agonists as needed for symptoms. ■ Intensity of treatment will depend on severity of exacerbation; see component 3-Managing Exacerbations. ■ Use of short-acting inhaled beta₂-agonists more than 2 times a week may indicate the need to initiate long-term-control therapy. 	<ul style="list-style-type: none"> ■ Teach basic facts about asthma ■ Teach inhaler/spacer/holding chamber technique ■ Discuss roles of medications ■ Develop self-management plan ■ Develop action plan for when and how to take rescue actions, especially for patients with a history of severe exacerbations ■ Discuss appropriate environmental control measures to avoid exposure to known allergens and irritants (See component 4.)

Step down
Review treatment every 1 to 6 months; a gradual stepwise reduction in treatment may be possible.

Step up
If control is not maintained, consider step up. First, review patient medication technique, adherence, and environmental control (avoidance of allergens or other factors that contribute to asthma severity).

NOTE:

- The stepwise approach presents general guidelines to assist clinical decisionmaking; it is not intended to be a specific prescription. Asthma is highly variable; clinicians should tailor specific medication plans to the needs and circumstances of individual patients.
- Gain control as quickly as possible; then decrease treatment to the least medication necessary to maintain control. Gaining control may be accomplished by either starting treatment at the step most appropriate to the initial severity of the condition or starting at a higher level of therapy (e.g., a course of systemic corticosteroids or higher dose of inhaled corticosteroids).
- A rescue course of systemic corticosteroids may be needed at any time and at any step.
- Some patients with intermittent asthma experience severe and life-threatening exacerbations separated by long periods of normal lung function and no symptoms. This may be especially common with exacerbations provoked by respiratory infections. A short course of systemic corticosteroids is recommended.
- At each step, patients should control their environment to avoid or control factors that make their asthma worse (e.g., allergens, irritants); this requires specific diagnosis and education.
- Referral to an asthma specialist for consultation or comanagement is recommended if there are difficulties achieving or maintaining control of asthma or if the patient requires step 4 care. Referral may be considered if the patient requires step 3 care (see also component 1-Initial Assessment and Diagnosis).

FIGURE 3-5a. USUAL DOSAGES FOR LONG-TERM-CONTROL MEDICATIONS

Medication	Dosage Form	Adult Dose	Child Dose	Comments
<i>Inhaled Corticosteroids</i> (see figures 3-5b and 3-5c)				
<i>Systemic Corticosteroids</i>			(Applies to all three systemic corticosteroids)	
Methylprednisolone	2, 4, 8, 16, 32 mg tablets	<ul style="list-style-type: none"> 7.5–60 mg daily in a single dose or qod as needed for control 	<ul style="list-style-type: none"> 0.25–2 mg/kg daily in single dose or qod as needed for control 	<ul style="list-style-type: none"> For long-term treatment of severe persistent asthma, administer single dose in a.m. either daily or on alternate days (alternate-day therapy may produce less adrenal suppression). If daily doses are required, one study suggests improved efficacy and no increase in adrenal suppression when administered at 3:00 p.m. (Beam et al. 1992). Short courses or "bursts" are effective for establishing control when initiating therapy or during a period of gradual deterioration. The burst should be continued until patient achieves 80% PEF personal best or symptoms resolve. This usually requires 3–10 days but may require longer. There is no evidence that tapering the dose following improvement prevents relapse.
Prednisolone	5 mg tablets, 5 mg/5 cc, 15 mg/5 cc	<ul style="list-style-type: none"> Short-course "burst": 40–60 mg per day as single or 2 divided doses for 3–10 days 	<ul style="list-style-type: none"> Short course "burst": 1–2 mg/kg/day, maximum 60 mg/day, for 3–10 days 	
Prednisone	1, 2.5, 5, 10, 20, 25 mg tablets; 5 mg/cc, 5 mg/5 cc			
<i>Cromolyn and Nedocromil</i>				
Cromolyn	MDI 1 mg/puff Nebulizer solution 20 mg/ampule	2–4 puffs tid-qid 1 ampule tid-qid	1–2 puffs tid-qid 1 ampule tid-qid	<ul style="list-style-type: none"> One dose prior to exercise or allergen exposure provides effective prophylaxis for 1–2 hours.
Nedocromil	MDI 1.75 mg/puff	2–4 puffs bid-qid	1–2 puffs bid-qid	<ul style="list-style-type: none"> See cromolyn above.
<i>Long-Acting Beta₂-Agonists</i>				
Salmeterol	<i>Inhaled</i> MDI 21 mcg/puff, 60 or 120 puffs DPI 50 mcg/blister	2 puffs q 12 hours 1 blister q 12 hours	1–2 puffs q 12 hours 1 blister q 12 hours	<ul style="list-style-type: none"> May use one dose nightly for symptoms. Should not be used for symptom relief or for exacerbations.
Sustained-Release Albuterol	<i>Tablet</i> 4 mg tablet	4 mg q 12 hours	0.3–0.6 mg/kg/day, not to exceed 8 mg/day	
<i>Methylxanthines</i>				
Theophylline	Liquids, sustained-release tablets, and capsules	Starting dose 10 mg/kg/day up to 300 mg max; usual max 800 mg/day	Starting dose 10 mg/kg/day; usual max: <ul style="list-style-type: none"> <1 year of age: 0.2 (age in weeks) + 5 = mg/kg/day ≥1 year of age: 16 mg/kg/day 	<ul style="list-style-type: none"> Adjust dosage to achieve serum concentration of 5–15 mcg/mL at steady-state (at least 48 hours on same dosage). Due to wide interpatient variability in theophylline metabolic clearance, routine serum theophylline level monitoring is important. See factors on page 87 that can affect levels.
<i>Leukotriene Modifiers</i>				
Zafirlukast	20 mg tablet	40 mg daily (1 tablet bid)		<ul style="list-style-type: none"> For zafirlukast, administration with meals decreases bioavailability; take at least 1 hour before or 2 hours after meals. For zileuton, monitor hepatic enzymes (ALT).
Zileuton	300 mg tablet 600 mg tablet	2,400 mg daily (two 300 mg tablets or one 600 mg tablet, qid)		

FIGURE 3-5a. USUAL DOSAGES FOR LONG-TERM-CONTROL MEDICATIONS (CONTINUED)

Factors Affecting Serum Theophylline Concentrations*			
Factor	Decreases Theophylline Concentrations	Increases Theophylline Concentrations	Recommended Action
Food	↓ or delays absorption of some sustained-release theophylline (SRT) products	↑ rate of absorption (fatty foods) products	Select theophylline preparation that is not affected by food.
Diet	↑ metabolism (high protein)	↓ metabolism (high carbohydrate)	Inform patients that major changes in diet are not recommended while taking theophylline.
Systemic, febrile viral illness (e.g., influenza)		↓ metabolism	Decrease theophylline dose according to serum concentration level. Decrease dose by 50 percent if serum concentration measurement is not available.
Hypoxia, cor pulmonale, and decompensated congestive heart failure, cirrhosis		↓ metabolism	Decrease dose according to serum concentration level.
Age	↑ metabolism (1 to 9 years)	↓ metabolism (<6 months, elderly)	Adjust dose according to serum concentration level.
Phenobarbital, phenytoin, carbamazepine	↑ metabolism		Increase dose according to serum concentration level.
Cimetidine		↓ metabolism	Use alternative H ₂ blocker (e.g., famotidine or ranitidine).
Macrolides: TAO, erythromycin, clarithromycin		↓ metabolism	Use alternative antibiotic or adjust theophylline dose.
Quinolones: ciprofloxacin, enoxacin, pefloxacin		↓ metabolism	Use alternative antibiotic or adjust theophylline dose. Circumvent with ofloxacin if quinolone therapy is required.
Rifampin	↑ metabolism		Increase dose according to serum concentration level.
Ticlopidine		↓ metabolism	Decrease dose according to serum concentration level.
Smoking	↑ metabolism		Advise patient to stop smoking; increase dose according to serum concentration level.

* This list is not all-inclusive; for discussion of other factors, see package inserts.

25 percent every 2 to 3 months to the lowest dose possible required to maintain control. It is likely that most patients with persistent asthma will continue to benefit from daily medication to suppress underlying airway inflammation. Patients may relapse when inhaled corticosteroids are completely discontinued (Waalkens et al. 1993).

Regular followup visits (at 1- to 6-month intervals) are essential. Clinicians need to assess whether control of asthma has been maintained and if a step down in therapy is appropriate. Clinicians also need to monitor and review the daily self-management and action plans, the medications, and the patient's self-management behaviors (e.g., inhaler and peak flow monitoring techniques, actions to control factors that aggravate their asthma) (see figure 4-2).

The Expert Panel *recommends* referral to an asthma specialist for consultation or comanagement of the patient if: there are difficulties achieving or maintaining control of asthma; immunotherapy is being considered; the patient requires step 4 care (step 3 or 4 care for infants and young children); or the patient has had a life-threatening exacerbation (see component 1-Initial Assessment and Diagnosis). Referral may be *considered* if a patient requires step 3 care (or step 2 care for infants and young children).

Pharmacologic Steps

The following recommendations for pharmacologic therapy at different steps of asthma severity (see figures 3-4a and 3-4b) are intended to be general guidelines for making therapeutic decisions. They are not

FIGURE 3-5b. ESTIMATED COMPARATIVE DAILY DOSAGES FOR INHALED CORTICOSTEROIDS

Adults			
Drug	Low Dose	Medium Dose	High Dose
Beclomethasone dipropionate 42 mcg/puff 84 mcg/puff	168-504 mcg (4-12 puffs — 42 mcg) (2-6 puffs — 84 mcg)	504-840 mcg (12-20 puffs — 42 mcg) (6-10 puffs — 84 mcg)	>840 mcg (>20 puffs — 42 mcg) (>10 puffs — 84 mcg)
Budesonide DPI: 200 mcg/dose	200-400 mcg (1-2 inhalations)	400-600 mcg (2-3 inhalations)	>600 mcg (>3 inhalations)
Flunisolide 250 mcg/puff	500-1,000 mcg (2-4 puffs)	1,000-2,000 mcg (4-8 puffs)	>2,000 mcg (>8 puffs)
Fluticasone MDI: 44, 110, 220 mcg/puff DPI: 50, 100, 250 mcg/dose	88-264 mcg (2-6 puffs — 44 mcg) OR (2 puffs — 110 mcg) (2-6 inhalations — 50 mcg)	264-660 mcg (2-6 puffs — 110 mcg) (3-6 inhalations — 100 mcg)	>660 mcg (>6 puffs — 110 mcg) OR (>3 puffs — 220 mcg) (>6 inhalations — 100 mcg) OR (>2 inhalations — 250 mcg)
Triamcinolone acetonide 100 mcg/puff	400-1,000 mcg (4-10 puffs)	1,000-2,000 mcg (10-20 puffs)	>2,000 mcg (>20 puffs)
Children			
Drug	Low Dose	Medium Dose	High Dose
Beclomethasone dipropionate 42 mcg/puff 84 mcg/puff	84-336 mcg (2-8 puffs — 42 mcg) (1-4 puffs — 84 mcg)	336-672 mcg (8-16 puffs — 42 mcg) (4-8 puffs — 84 mcg)	>672 mcg (>16 puffs — 42 mcg) (>8 puffs — 84 mcg)
Budesonide DPI: 200 mcg/dose	100-200 mcg	200-400 mcg (1-2 inhalations — 200 mcg)	>400 mcg (>2 inhalations — 200 mcg)
Flunisolide 250 mcg/puff	500-750 mcg (2-3 puffs)	1,000-1,250 mcg (4-5 puffs)	>1,250 mcg (>5 puffs)
Fluticasone MDI: 44, 110, 220 mcg/puff DPI: 50, 100, 250 mcg/dose	88-176 mcg (2-4 puffs — 44 mcg) (2-4 inhalations — 50 mcg)	176-440 mcg (4-10 puffs — 44 mcg) OR (2-4 puffs — 110 mcg) (2-4 inhalations — 100 mcg)	>440 mcg (>4 puffs — 110 mcg) OR (>2 puffs — 220 mcg) (>4 inhalations — 100 mcg) OR (>2 inhalations — 250 mcg)
Triamcinolone acetonide 100 mcg/puff	400-800 mcg (4-8 puffs)	800-1,200 mcg (8-12 puffs)	>1,200 mcg (>12 puffs)
Note:			
<ul style="list-style-type: none"> ■ The most important determinant of appropriate dosing is the clinician's judgment of the patient's response to therapy. The clinician must monitor the patient's response on several clinical parameters and adjust the dose accordingly. The stepwise approach to therapy emphasizes that once control of asthma is achieved, the dose of medication should be carefully titrated to the minimum dose required to maintain control, thus reducing the potential for adverse effect. ■ See figure 3-5c for an explanation of the rationale used for the comparative dosages. The reference point for the range in the dosages for children is data on the safety of inhaled corticosteroids in children, which, in general, suggest that the dose ranges are equivalent to beclomethasone dipropionate 200-400 mcg/day (low dose), 400-800 mcg/day (medium dose), and >800 mcg/day (high dose). ■ Some dosages may be outside package labeling. ■ Metered-dose inhaler (MDI) dosages are expressed as the actuator dose (the amount of drug leaving the actuator and delivered to the patient), which is the labeling required in the United States. This is different from the dosage expressed as the valve dose (the amount of drug leaving the valve, all of which is not available to the patient), which is used in many European countries and in some of the scientific literature. Dry powder inhaler (DPI) doses are expressed as the amount of drug in the inhaler following activation. 			