

Review article

Asthma management pocket reference 2008*

Asthma is one of the most common chronic airways diseases worldwide, and its prevalence is increasing. Family doctors (sometimes called 'primary care physicians' or 'general practitioners') are frequently an asthma patient's first point of contact with healthcare systems. Disease management that follows evidence-based practice guidelines yields better patient results, but such guidelines are often complicated and may recommend the use of resources not available in the family practice setting. A joint expert panel of the World Organization of Family Doctors (Wonca), International Primary Care Airways Group (IPAG) and the International Primary Care Respiratory Group (IPCRG) offers support to family doctors worldwide by distilling the globally accepted, evidence-based recommendations from the Global Initiative for Asthma (GINA) into this brief reference guide. This guide provides tools intended to supplement a thorough history taking and the clinician's professional judgment in order to provide the best possible care for patients with asthma. Diagnostic Questionnaires developed for children and adults specifically focus the physician's attention on key symptoms and markers of asthma. When questionnaire responses suggest a diagnosis of asthma, Diagnosis Guides then lead the clinician through a series of investigations commonly available in primary care to support the diagnosis. In patients >40 years who smoke, COPD is an important alternative diagnosis, and some key aspects of differential diagnosis are illuminated. According to GINA, the goal of asthma treatment is to achieve and maintain control of the disease symptoms long-term. The physician must first assess the patient's current level of asthma control, then treat asthma in a stepwise manner to achieve and maintain symptom control. Both of these aspects are summarized in figures included in this guide. Finally, the guide also presents a flow chart summarizing management of asthma exacerbations in the acute care setting, and a glossary of asthma medications to assist the clinician in making medication choices for each individual patient. Finally, many patients with asthma also have concomitant allergic rhinitis, and this must be checked. The World Organization of Family Doctors has been delegated by WHO as the group that will be taking primary responsibility for education about chronic respiratory diseases among primary care physicians globally. This document will be a major resource in this educational program.

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The purpose of this guide

Management that follows evidence-based practice guidelines yields better patient results. However, global evidence-based practice guidelines are often complicated and recommend the use of resources often not available in the family practice setting worldwide. The prevalence of asthma in family practice is high. In some groups of patients, such as smokers over 40 years, COPD may be more prevalent than asthma. This raises the issues of differential diagnosis, as treatment strategies for asthma and COPD are different. The joint Wonca/GARD expert panel offers support to family doctors† worldwide by distilling the Global Initiative for Asthma (GINA) and International Primary Care Airways Group (IPAG) recommendations into this brief reference guide. The guide lists diagnostic and therapeutic measures, which can be carried out in the family medicine environment and in this way it is intended to improve the quality of care for patients with asthma in primary care. This document was prepared by the Wonca Expert Panel including C. van Weel, E. D. Bateman, J. Bousquet, J. Reid, L. Grouse, T. Schermer, E. Valovirta, N. Zhong, and was edited by Dmitry Nonikov. The authors acknowledge the contribution of International Primary Care Respiratory Group (IPCRG), the European Federation of Allergy and Airways Diseases Patients Associations (EFA), and the GINA, who supported the development with their review and input.

Diagnosing asthma

The questionnaires and diagnosis guides supplied below have been specially adapted to facilitate the diagnosis of asthma in primary care. History taking of patients with respiratory and allergy-related problems should be based on the general principles of history taking in primary care. Family doctors should first and foremost apply active listening and then invite patients to express their symptoms, worries and concerns. This will often present a full picture. Validated questionnaires are not intended to replace history taking, but identify key symptoms and elements of the medical history to explore with patients. The investigations presented in the diagnosis guides may not be available in all areas; in most cases, the combination of those diagnostic investigations that are available and the individual healthcare professional’s clinical judgment will lead to an accurate clinical diagnosis. The guides are intended to supplement, not replace, a complete physical examination and thorough medical history. For patients

†In different healthcare systems, the terms ‘primary care physicians’ or ‘general practitioners’ may be used.

diagnosed with asthma, it is important to assess whether they also have allergic rhinitis, a common comorbidity.

Childhood asthma questionnaire (1)

Interpretation

Question	Response Choices	
1. Have you/has your child had wheezing or whistling in the chest in the last 12 months?	Yes	No
2. In the last 12 months, have you/has your child had a dry cough at night, apart from a cough associated with a cold or chest infection?	Yes	No
3. Do you/does your child have a history of hay fever or eczema?	Yes	No
4. Is there a family history of asthma in your (child's) first-degree relatives?	Yes	No
5. Have you/has your child received more than three courses of antibiotics for respiratory symptoms (both upper and lower respiratory tract) in the last 12 months?	Yes	No
6. In the last 12 months, has your (child's) chest sounded wheezy during or after exercise?	Yes	No
7. In the last 12 months, has your (child's) sleep been disturbed due to wheezing?	Yes	No
8. In the last 12 months, has wheezing ever been severe enough to limit your (child's) speech to only one or two words at a time between breaths?	Yes	No
9. In the last 12 months, have you/has your child been to a doctor, an emergency room, or a hospital for wheezing?	Yes	No

In children aged 6–14 years, a positive response to any of the questions above suggests an increased likelihood of asthma, and suggests that the patient should undergo further diagnostic assessment. Positive responses to three or more of the questions in bold suggest a >90% likelihood of asthma. If responses suggest asthma, proceed to the Childhood Asthma Diagnosis Guide below. If responses suggest that asthma is unlikely, consider alternative diagnoses and/or referral to a specialist.

Childhood asthma diagnosis guide (1)

Diagnostic Tool	Findings that Support Diagnosis
Physical examination	• Expiratory wheeze on auscultation (may or may not be present). • Increased expiratory time (may or may not be present).
Reversibility testing with spirometry or PEF	Demonstration of reversible airflow limitation: • FEV₁ improves at least 12% or 200 mL either spontaneously, 15 minutes after inhaled bronchodilator, or after trial of glucocorticosteroid therapy; OR • PEF improves at least 60 L/min (or 20% or more of pre-bronchodilator PEF) after inhalation of a bronchodilator.
Exercise challenge with spirometry or PEF	Demonstration of airway hyperresponsiveness Note: Some children with asthma present only with symptoms associated with exercise.
Home PEF diary (if needed)	Demonstration of variable airflow limitation: • Diurnal variation in PEF of more than 20% (with twice-daily readings, more than 10%).
Trial of therapy	Improvement with bronchodilators or with trial of inhaled glucocorticosteroid therapy.
Allergy skin testing or measurement of allergen-specific IgE in serum	• Confirm presence of atopy. • Specific triggers identified.

Adult asthma questionnaire (1)

Interpretation

Question	Response Choices	
1. Have you had wheezing or whistling in your chest at any time in the last 12 months?	Yes	No
2. Have you been woken up at night by an attack of shortness of breath at any time in the last 12 months?	Yes	No
3. Have you been woken up at night by an attack of coughing at any time in the last 12 months?	Yes	No
4. Have you woken up with a feeling of tightness in your chest at any time in the last 12 months?	Yes	No
5. Have you had an attack of shortness of breath that came on following strenuous activity at any time?	Yes	No
6. Have you had an attack of shortness of breath that came on during the day when you were at rest at any time?	Yes	No
7. If you answered "Yes" to any of the questions above, do your symptoms occur less frequently or not at all on days away from work and on vacations?	Yes	No

A positive response to any of the questions 1–6, particularly questions one or two in bold, suggests an increased likelihood of asthma. The more the number of positive answers, the greater the likelihood of asthma. If in your judgment, the patient's responses suggest asthma, proceed to the Adult Asthma Diagnosis Guide below. A positive response to question 7 suggests an occupational association. Referral of the patient to a specialist for further objective testing and assessment is recommended. If answers suggest that asthma is unlikely, consider other diagnoses or specialist referral.

Adult asthma diagnosis guide (1)

Diagnostic Tool	Findings that Support Diagnosis
Medical history	In addition to the information elicited in the Adult Asthma Questionnaire, the following features tend to be characteristic but do not occur in every case: - Onset early in life (often childhood) - Symptoms vary from day to day - Symptoms at night/early morning - Allergy, rhinitis, and/or eczema also present - Family history of asthma.
Physical examination	- Expiratory wheeze on auscultation (may or may not be present). - Increased expiratory time (may or may not be present). - Hyperinflation (may or may not be present).
Reversibility testing with spirometry or PEF	Demonstration of reversible airflow limitation: - FEV₁ improves at least 12% or 200 ml either spontaneously, 15 minutes after inhaled bronchodilator, or after trial of glucocorticosteroid therapy; OR - PEF improves at least 60 L/min (or 20% or more of pre-bronchodilator PEF) after inhalation of a bronchodilator. (Note: Postbronchodilator FEV ₁ /FVC < 0.70 suggests COPD.)
Exercise challenge with spirometry or PEF	Demonstration of airway hyperresponsiveness.
Home PEF diary (if needed)	Demonstration of variable airflow limitation: Diurnal variation in PEF of more than 20% (with twice-daily readings, more than 10%).
Trial of therapy	Improvement with bronchodilators or with trial of glucocorticosteroid therapy.
Allergy skin testing or measurement of allergen-specific IgE in serum	- Confirm presence of atopy. - Specific triggers identified.

Differential diagnosis with COPD

Among adult patients, it is important to exclude the diagnosis of COPD in making the diagnosis of asthma.

HISTORY	COPD	ASTHMA	INVESTIGATIONS	COPD	ASTHMA
Smoker or ex-smoker	Nearly always	Variable	FEV ₁	Always Reduced, Except Stage 1	Variable
Frequent respiratory symptoms in childhood	Infrequent	Often	Daily Variations in PEF	Minimal	"Morning dip" + day to day
Chronic Cough and Sputum	Common	Infrequent	Objective Response to SABA	Nil / Partial	Partial / Complete
Breathlessness	Gradual and Progressive	Intermittent, except persistent asthma	Objective Response to Corticosteroid Trial	Partial Response in 10–20%	Good Response in Majority
Age	> 45	Any / Early in life			

Treating to achieve control

Once asthma is diagnosed, it is important to provide treatment that will control patient symptoms.

Key points:

- Effective and safe pharmacological regimens are available for asthma. Pharmacological treatment is the primary component of asthma management.
- Education is essential for the patients to increase compliance with therapy.
- Allergen avoidance may be indicated in specific patients.

Each patient is assigned to one of five treatment 'steps'. These detail the treatments at each step for adults and children age 5 and over.

At each treatment step, reliever medication should be provided for quick relief of symptoms as needed (however, be aware of how much reliever medication the patient is using – regular or increased use indicates that asthma is not well controlled). At steps 2 through 5, patients also require one or more regular controller medications, which keep symptoms and attacks from starting. Controller medications include inhaled and systemic glucocorticosteroids, leukotriene modifiers, long-acting inhaled beta-2-agonists in combination with inhaled glucocorticosteroids, sustained-release theophylline, anti-IgE, and other systemic steroid-sparing therapies. Inhaled glucocorticosteroids are currently the most effective anti-inflammatory medications for the treatment of persistent asthma. Their therapeutic index is always more favorable than long-term systemic glucocorticosteroids in asthma. Long-term oral glucocorticosteroid therapy may be required for severe uncontrolled asthma, but its use is limited by the risk of significant adverse effects.

The available literature on treatment of asthma in children 5 years and younger precludes detailed treatment

recommendations. The best documented treatment to control asthma in these age groups is inhaled glucocorticosteroids and at step 2, a low-dose inhaled glucocorticosteroid is recommended as the initial controller treatment.

Assessing asthma control

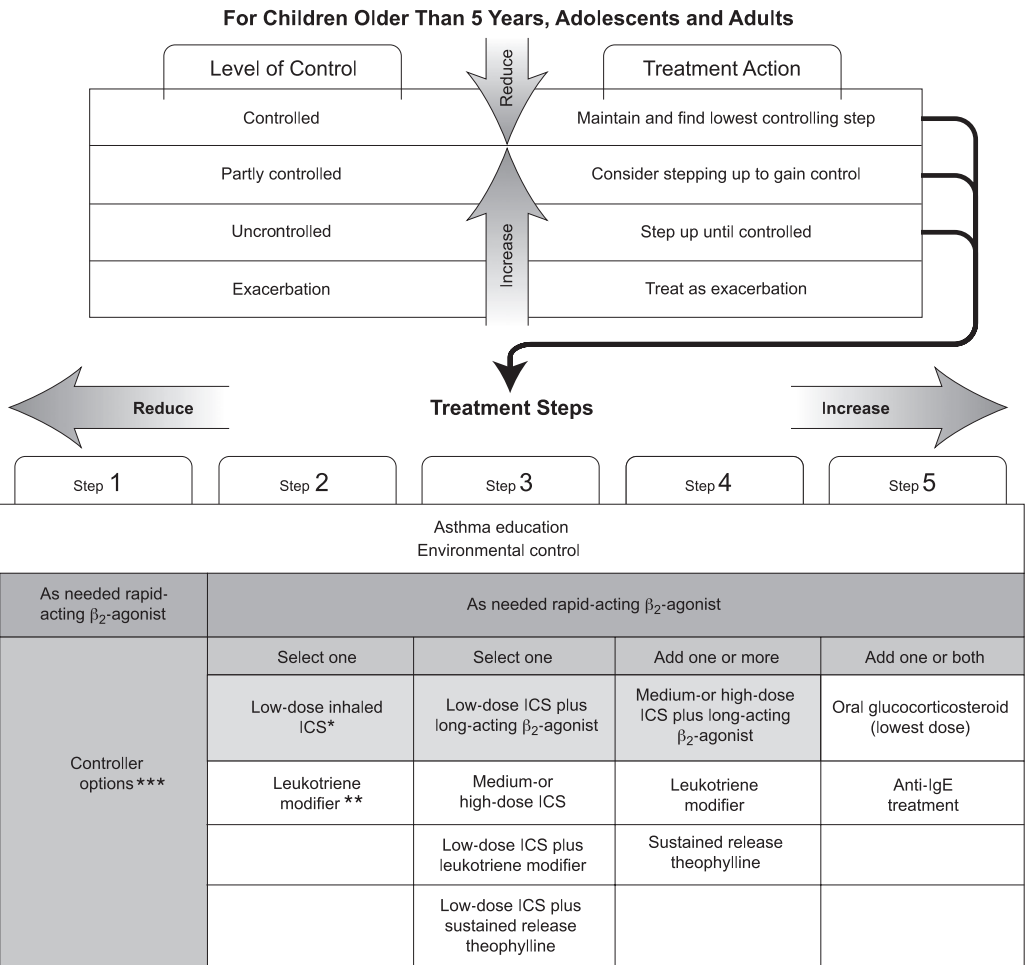
Each patient should be assessed to establish his or her current treatment regimen, adherence to the current regimen, and level of asthma control. The need for rescue medication (addressed by questions such as ‘How often do you have to puff on your blue canister?’) is an important factor for assessing asthma control in family medicine. A simplified scheme for recognizing controlled, partly controlled, and uncontrolled asthma is provided in the figure below.

Characteristic	Controlled (All of the following)	Partly Controlled (Any measure present in any week)	Uncontrolled
Daytime symptoms	None (twice or less/week)	More than twice/week	Three or more features of partly controlled asthma present in any week
Limitations of activities	None	Any	
Nocturnal symptoms/ awakening	None	Any	
Need for reliever/ rescue treatment	None (twice or less/week)	More than twice/week	
Lung function (PEF or FEV ₁) [‡]	Normal	< 80% predicted or personal best (if known)	One in any week [†]
Exacerbations	None	One or more/year*	

* Any exacerbation should prompt review of maintenance treatment to ensure that it is adequate.
† By definition, an exacerbation in any week makes that an uncontrolled asthma week.
‡ Lung function testing is not reliable for children 5 years and younger.

Management approach based on control

Total dose of topical steroids should be considered if intranasal steroids are used for concomitant allergic rhinitis.

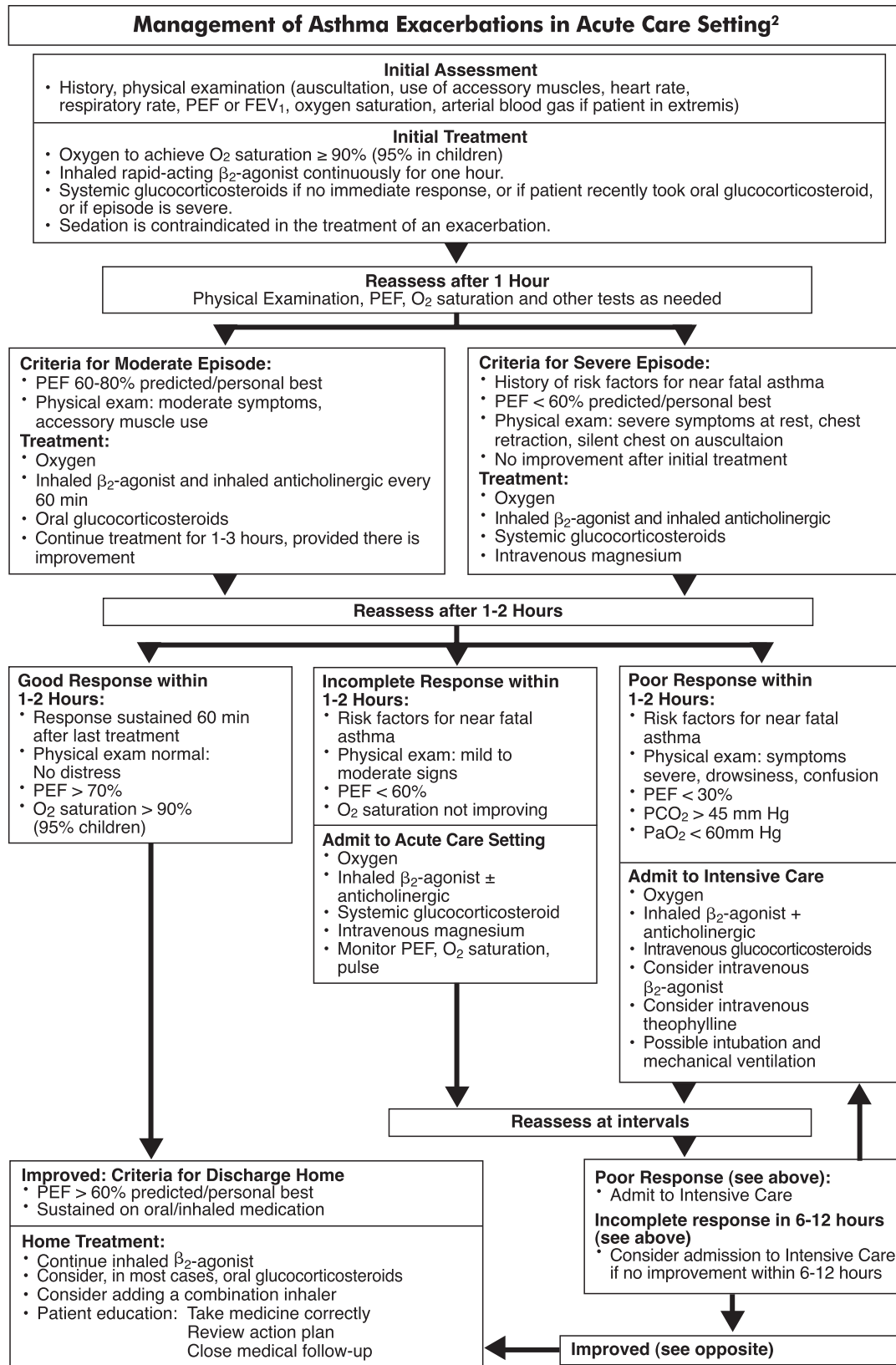


* ICS = inhaled glucocorticosteroids
** $\pm$ Receptor antagonist or synthesis inhibitors
*** = Preferred controller options are shown in shaded boxes

Total dose of topical steroids should be considered if intranasal steroids are used for concomitant allergic rhinitis. Alternative reliever treatments include inhaled anticholinergics, short-acting oral β_2 -agonists, some long-acting β_2 -agonists, and short-acting theophylline. Regular dosing with short and long-acting β_2 -agonist is not advised unless accompanied by regular use of an inhaled glucocorticosteroid.

²Global Initiative for Asthma. Full text GINA documents and resources: <http://www.ginasthma.org>.

Management of asthma exacerbations in acute care setting

²Global Initiative for Asthma. Full text GINA documents and resources: <http://www.ginasthma.org>.

Glossary of asthma medications – controllers

Name and Also Known As	Usual Doses	Side Effects	Comments
Glucocorticosteroids Adrenocorticoids Corticosteroids Glucocorticoids Inhaled (ICS): Beclomethasone Budesonide Ciclesonide Flunisolide Fluticasone Mometasone furoate Triamcinolone Tablets or syrups: hydrocortisone methylprednisolone prednisolone prednisone	Inhaled: Beginning dose dependent on asthma control then titrated down over 2-3 months to lowest effective dose once control is achieved. Tablets or syrups: For daily control use lowest effective dose 5-40 mg of prednisone equivalent in a.m. or qod. For acute attacks 40-60 mg daily in 1 or 2 divided doses for adults or 1-2 mg/kg daily in children.	Inhaled: High daily doses may be associated with skin thinning and bruises, and rarely adrenal suppression. Local side effects are hoarseness and oropharyngeal candidiasis. Low to medium doses have produced minor growth delay or suppression (av. 1 cm) in children. Attainment of predicted adult height does not appear to be affected. Tablets or syrups: Used long term, may lead to osteoporosis, hypertension, diabetes, cataracts, adrenal suppression, growth suppression, obesity, skin thinning or muscle weakness. Consider coexisting conditions that could be worsened by oral glucocorticosteroids, e.g. herpes virus infections, Varicella, tuberculosis, hypertension, diabetes and osteoporosis	Inhaled: Potential but small risk of side effects is well balanced by efficacy. Valved holding-chambers with MDIs and mouth washing with DPIs after inhalation decrease oral Candidiasis. Preparations not equivalent on per puff or μg basis. Tablet or syrup: Long term use: alternate day a.m. dosing produces less toxicity. Short term: 3-10 day "bursts" are effective for gaining prompt control.
Sodium cromoglycate cromolyn cromones	MDI 2 mg or 5 mg 2-4 inhalations 3-4 times daily. Nebulizer 20 mg 3-4 times daily.	Minimal side effects. Cough may occur upon inhalation.	May take 4-6 weeks to determine maximum effects. Frequent daily dosing required.
Nedocromil cromones	MDI 2 mg/puff 2-4 inhalations 2-4 times daily.	Cough may occur upon inhalation.	Some patients unable to tolerate the taste.
Long-acting β_2-agonists beta-adrenergics sympathomimetics LABAs Inhaled: Formoterol (F) Salmeterol (Sm) Sustained-release Tablets: Salbutamol (S) Terbutaline (T)	Inhaled: DPI-F: 1 inhalation (12 μg) bid. MDI-F: 2 puffs bid. DPI-Sm: 1 inhalation (50 μg) bid. MDI-Sm: 2 puffs bid. Tablets: S: 4 mg q12h. T: 10mg q12h.	Inhaled: fewer, and less significant, side effects than tablets. Have been associated with an increased risk of severe exacerbations and asthma deaths when added to usual therapy. Tablets: may cause tachycardia, anxiety, skeletal muscle tremor, headache, hypokalemia.	Inhaled: Salmeterol NOT to be used to treat acute attacks. Should not use as monotherapy for controller therapy. Always use as adjunct to ICS therapy. Formoterol has onset similar to salbutamol and has been used as needed for acute symptoms. Tablets: As effective as sustained-release theophylline. No data for use as adjunctive therapy with inhaled glucocorticosteroids.
Combination ICS/LABA Fluticasone/ salmeterol (F/S) Budesonide/ formoterol (B/F)	DPI-F/S 100, 250, or 500 μg /50 μg 1 inhalation bid MDI-F/S 50, 125, or 250 μg /25 μg 2 puffs bid DPI-B/F 100 or 200 μg /6 μg 1 inhalation bid MDI-B/F 80 or 160 μg /4.5 μg 2 puffs bid	Similar to those described above for individual components of the combination	In moderate to severe persistent asthma, combination more effective than doubling the ICS dose. Budesonide/formoterol has been approved for adjustable as needed dosing in addition to regular dosing in some countries. Dosing is dependent on level of control. Limited data in children 4-11 yrs. No data in children < 4 yrs.

Glossary ... (continued)

Name and Also Known As	Usual Doses	Side Effects	Comments
Sustained-release Theophylline Aminophylline methylxanthine xanthine	Starting dose 10 mg/kg/day with usual 800 mg maximum in 1-2 divided doses.	Nausea and vomiting are most common. Serious effects occurring at higher serum concentrations include seizures, tachycardia, and arrhythmias.	Theophylline level monitoring is often required. Absorption and metabolism may be affected by many factors, including febrile illness.
Antileukotrienes Leukotriene modifiers Montelukast (M) Pranlukast (P) Zafirlukast (Z) Zileuton (Zi)	Adults: M 10mg qhs P 450mg bid Z 20mg bid; Zi 600mg qid. Children: M 5 mg qhs (6-14 y) M 4 mg qhs (2-5 y) Z 10mg bid (7-11 y)	No specific adverse effects to date at recommended doses. Elevation of liver enzymes with Zafirlukast and Zileuton and limited case reports of reversible hepatitis and hyperbilirubinemia with Zileuton and hepatic failure with Zafirlukast	Antileukotrienes are most effective for patients with mild persistent asthma. They provide additive benefit when added to ICSs though not as effective as inhaled long-acting β_2 -agonists.
Immunomodulators Omalizumab Anti-IgE	Adults: Dose administered subcutaneously every 2 or 4 weeks dependent on weight and IgE concentration	Pain and bruising at injection site (5-20%) and very rarely anaphylaxis (0.1%).	Need to be stored under refrigeration 2-8°C and maximum of 150 mg administered per injection site.

Glossary of asthma medications – relievers

Name and Also Known As	Usual Doses	Side Effects	Comments
Short-acting β_2-agonists Adrenergics β_2 -stimulants Sympathomimetics Albuterol/salbutamol Fenoterol Levalbuterol Metaproterenol Pirbuterol Terbutaline	Differences in potency exist but all products are essentially comparable on a per puff basis. For prn symptomatic use and pretreatment before exercise 2 puffs MDI or 1 inhalation DPI. For asthma attacks 4-8 puffs q2-4h, may administer q20min x 3 with medical supervision or the equivalent of 5 mg salbutamol by nebulizer.	Inhaled: tachycardia, skeletal muscle tremor, headache, and irritability. At very high dose hyperglycemia, hypokalemia. Systemic administration as Tablets or Syrup increases the risk of these side effects.	Drug of choice for acute bronchospasm. Inhaled route has faster onset and is more effective than tablet or syrup. Increasing use, lack of expected effect, or use of > 1 canister a month indicate poor asthma control; adjust long-term therapy accordingly. Use of ≥ 2 canisters per month is associated with an increased risk of a severe, life-threatening asthma attack.
Anticholinergics Ipratropium bromide (IB) Oxitropium bromide	IB-MDI 4-6 puffs q6h or q20 min in the emergency department. Nebulizer 500 μ g q20min x 3 then q2-4hrs for adults and 250-500 μ g for children.	Minimal mouth dryness or bad taste in the mouth.	May provide additive effects to β_2 -agonist but has slower onset of action. Is an alternative for patients with intolerance for β_2 -agonists.
Short-acting theophylline Aminophylline	7 mg/kg loading dose over 20 min followed by 0.4 mg/kg/hr continuous infusion.	Nausea, vomiting, headache. At higher serum concentrations: seizures, tachycardia, and arrhythmias.	Theophylline level monitoring is required. Obtain serum levels 12 and 24 hours into infusion. Maintain between 10-15 μ g/mL.
Epinephrine/adrenaline injection	1:1000 solution (1mg/mL). 0.1mg/kg up to 0.3-0.5 mg, can give q20min x 3.	Similar, but more significant effects than selective β_2 -agonist. In addition: hypertension, fever, vomiting in children and hallucinations.	In general, not recommended for treating asthma attacks if selective β_2 -agonists are available.

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