Asthma

Pharmacologic Therapy

General Approach

3- Table -2 depicts the **GINA stepwise approach for control-based management**.

Table 2:GINA Stepwise Approach to Control Symptoms and Minimize Future Risk

Step	Preferred Option (Evidence Level)	Other Recommended Options (Evidence Level)
1	As-needed SABA (A)	Consider low-dose ICS, in addition to as-needed SABA, for patients at risk for exacerbations (B)
2	Low-dose ICS plus as-needed SABA (A)	LTRA (A) Low-dose ICS/LABA (A) ICS started with symptoms of allergic asthma, for seasonal treatment only (D)
3	Low-dose ICS/LABA, plus as-needed SABA for adults/adolescents OR low-dose ICS/formoterol as both maintenance and reliever (A) For children 6–11 years of age, moderate-dose ICS, plus as-needed SABA	Medium-dose ICS for adults/adolescents (A) Low-dose ICS plus LTRA (A) or low-dose, sustained-release theophylline (B)

4	Medium-dose ICS/LABA, plus as-needed SABA for adults/adolescents (B) OR medium-dose ICS/formoterol as both maintenance and reliever (A) For children 6–11 years of age, refer child to asthma specialist	Add-on therapy with tiotropium for adults with exacerbation history (A) Sublingual allergen immunotherapy in adults with allergic rhinitis and house dust mite sensitization if FEV_1 is >70% predicted
5	Referral to specialist and consideration of add-on treatment if asthma remains uncontrolled	Add-on anticholinergic (B): tiotropium if ≥12 years of age Add-on anti-IgE (A): omalizumab (subcutaneous) for moderate-to-severe allergic asthma if ≥6 years of age Add-on anti-interleukin-5 therapy (A): mepolizumab if ≥12 years (subcutaneous); reslizumab if ≥18 years) (intravenous) Add-on anti-interleukin 5 receptor (A): benralizumab if ≥12 years (subcutaneous)

ICS, inhaled corticosteroids; LABA, long-acting β2 -agonist; LTRA, leukotriene receptor antagonist; OCS, oral corticosteroids; SABA, short-acting β2 -agonist. FEV, forced expiratory volume in 1 second

4-**Step-down of controller treatment may be considered** if symptoms have been well controlled and lung function has been stable for 3 months or longer.

5-Stepping down **inhaled corticosteroids (ICS) doses by 25%–50% at 3-month intervals** is feasible and safe for most patients.

6-The **primary therapy of acute exacerbations includes** inhaled **SABAs** and (depending on severity) **systemic corticosteroids**, inhaled **ipratropium**, intravenous (IV) **magnesium** sulfate (a bronchodilator. It relaxes the bronchial muscles and expands the airways), and **oxygen**.

Treatments are typically administered concurrently to facilitate rapid improvement.

β2-Agonists

1-**SABAs are the most effective bronchodilators**. **Aerosol administration** enhances bronchoselectivity and provides more rapid response and greater protection against provocations (eg, exercise, allergen challenges) **than systemic administration**.

2-Albuterol and other inhaled SABAs are indicated for **intermittent episodes** of bronchospasm and are the treatment of choice **for acute severe asthma and Exercise-induced bronchospasm (EIB).**

3-Two **long-acting β2-agonists** (**LABAs**), **formoterol** and **salmeterol**, provide bronchodilation for 12 hours or longer.

4-Combination treatment **with ICS/LABA provides greater asthma control** than increasing the dose of ICS alone **while reducing the frequency exacerbations**. A SABA should be continued for acute exacerbations.

Corticosteroids

1-**ICS are the preferred long-term control therapy for persistent asthma** because of potency and consistent effectiveness; they are the only therapy shown to reduce risk of dying from asthma.

2-**After asthma is controlled, many patients can reduce the ICS dose and maintain control**.

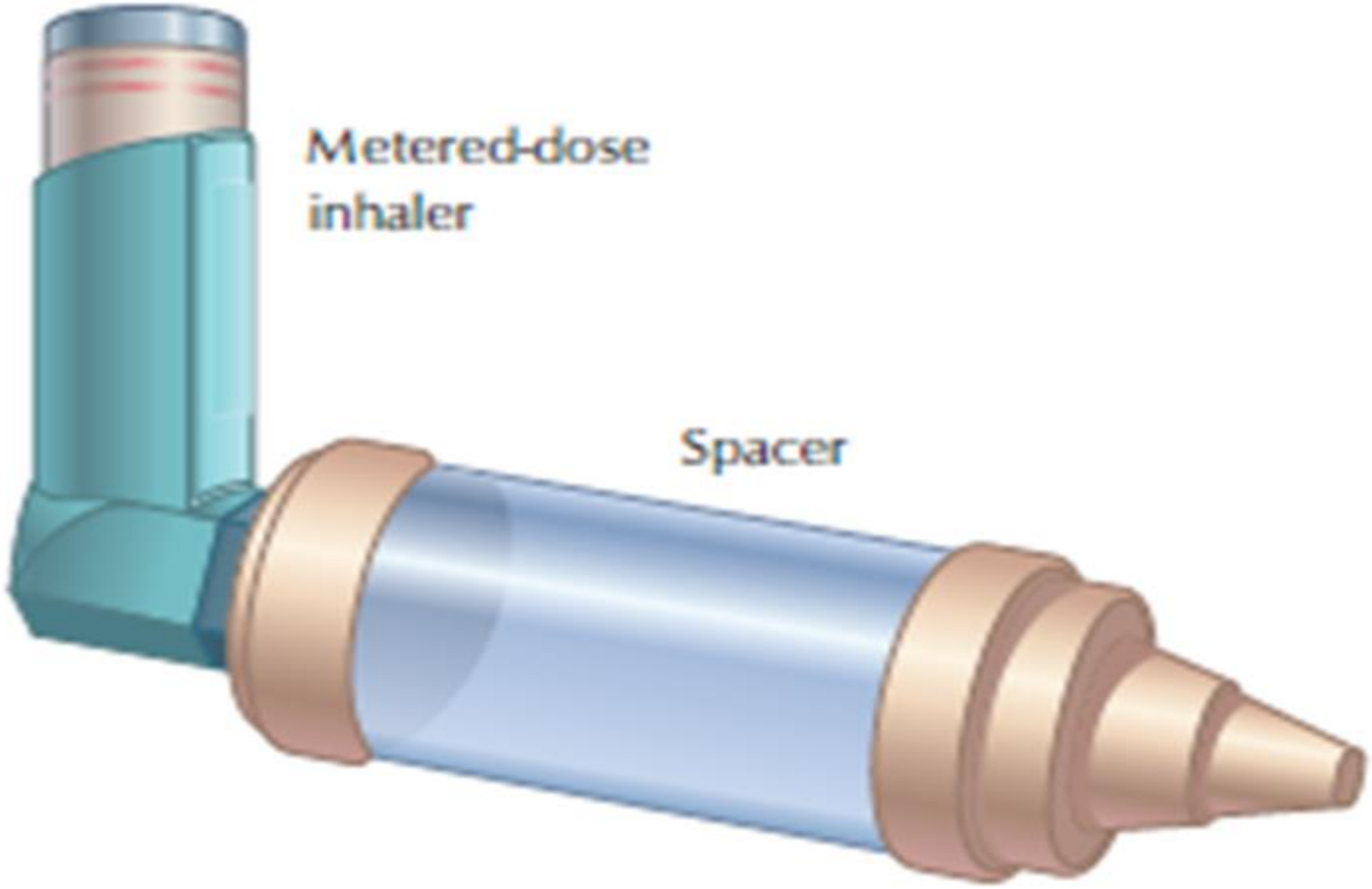
3-**Response to ICS is delayed**; **symptoms** improve in most patients within the first 1–2 weeks and reach maximum improvement in 4–8 weeks.

Maximum improvement **in FEV1** (forced expiratory volume in 1 second) and PEF (**Peak expiratory flows)** rates may require 3–6 weeks.

4-**Systemic toxicity of ICS is minimal with low-to-moderate doses**, but risk of systemic effects increases with high doses (eg, growth suppression in children, osteoporosis, cataracts, dermal thinning, adrenal insufficiency).

5-Local adverse effects include dose-dependent oropharyngeal **candidiasis** and dysphoniaبحة الصوت, which can be **reduced by using a spacer device** جهاز مباعد.

Spacer device



7-IV therapy offers no advantage over oral administration except in patients unable to take oral medications.

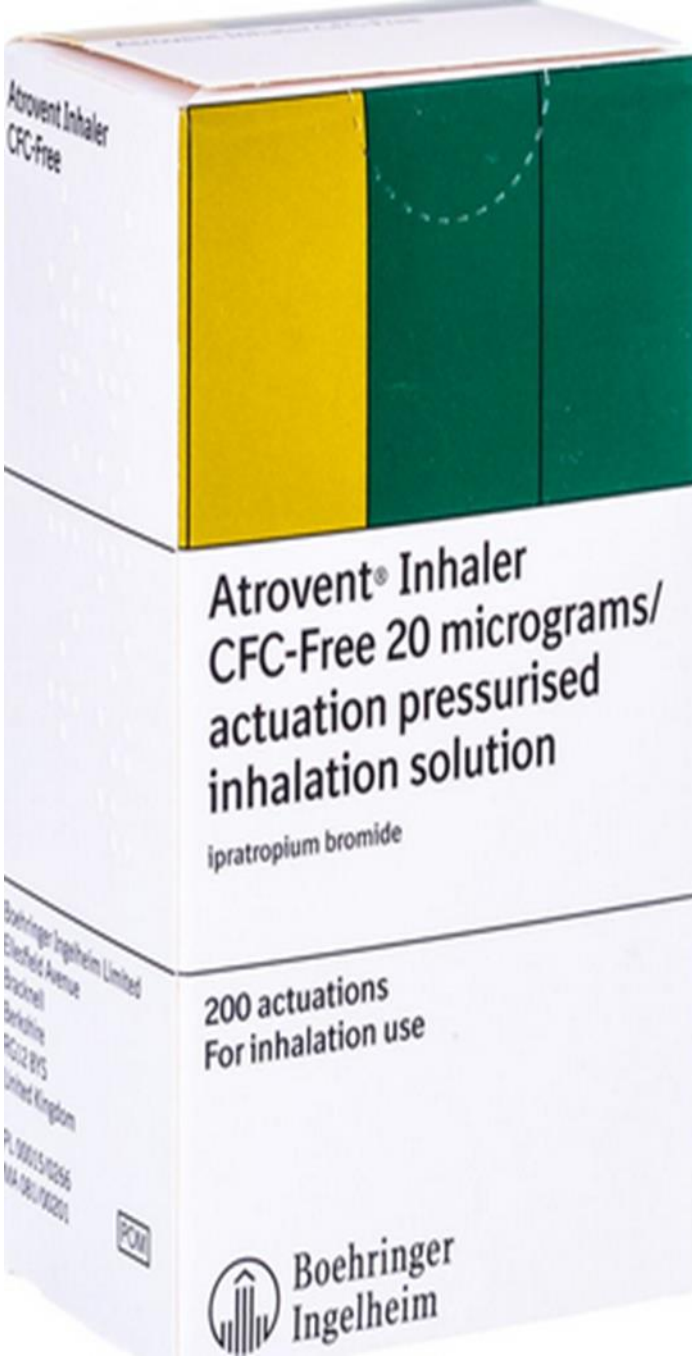
8-Adults are treated effectively with 5–7 days of oral prednisone (or equivalent), but **children may require only 3–5 days. Dexamethasone for 1–2 days is an option for children** and has the benefit of less vomiting. Continue full doses until the PEF **(Peak expiratory flows)** reaches 70% of predicted normal or personal best.

9-Because **short-term (1–2 weeks),** high-dose corticosteroids (1–2 mg/kg/day of oral prednisone) **do not produce serious toxicities**, the ideal strategy is to use **systemic corticosteroids in a short "burst" and then maintain the patient on appropriate long-term control therapy with ICS.**

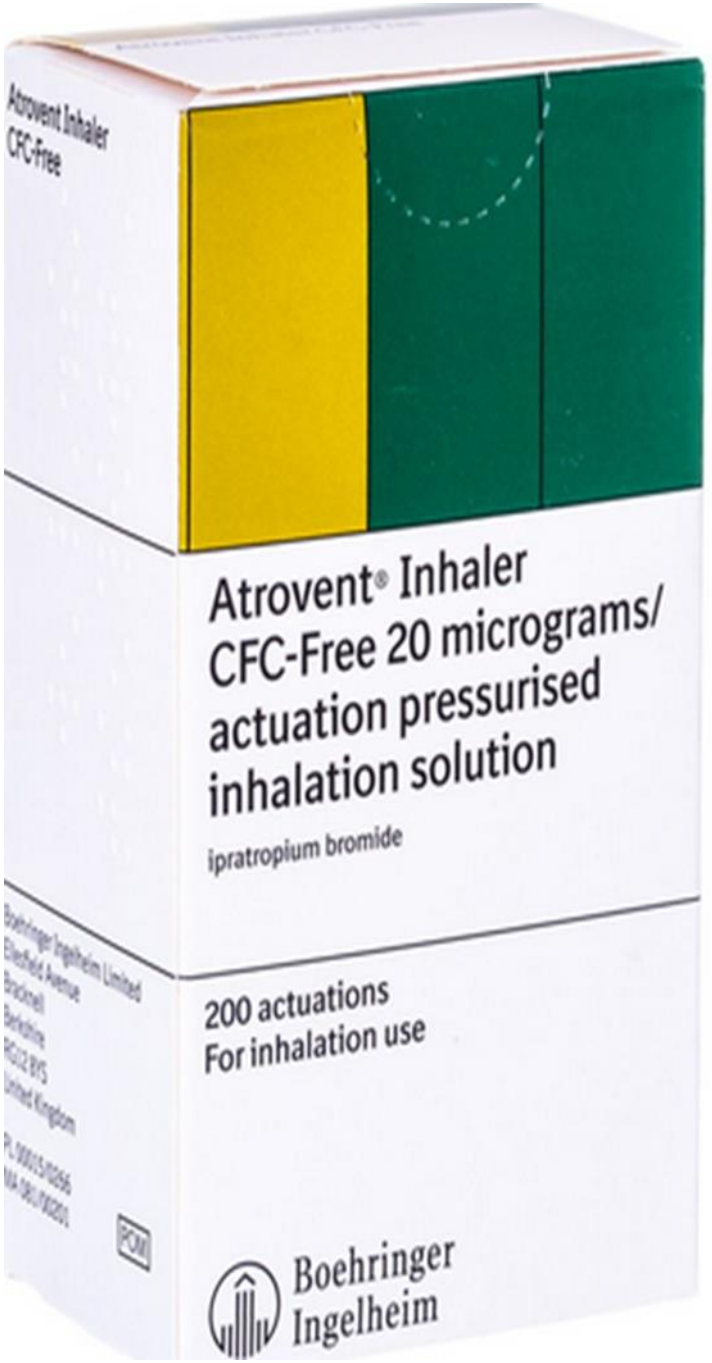
Anticholinergics

1-**Ipratropium** bromide and **tiotropium** bromide produce bronchodilation only in cholinergic-mediated bronchoconstriction.

Anticholinergics are effective bronchodilators **but are not as effective as β2-agonists.**



2-Ipratropium bromide is approved by the FDA for **maintenance treatment of bronchospasm associated with COPD** but is not currently approved for treatment of asthma.



3-Tiotropium bromide is also approved for once-daily **maintenance treatment of COPD** and is also indicated for the long-term, once-daily, **maintenance treatment of asthma** in patients ≥6 years of age.

4-Time to reach maximum bronchodilation from aerosolized **ipratropium is longer than from aerosolized SABAs** (30–60 minutes vs. 5–10 minutes). Ipratropium bromide has a duration of action of 4–8 hours; **tiotropium bromide has a duration of 24 hours.**

5-In acute asthma exacerbations, inhaled ipratropium bromide produces **a further improvement in lung function of 10%–15% over inhaled β2-agonists alone.**

6-Inhaled ipratropium bromide should only be considered as **adjunctive therapy** in acute severe **asthma not completely responsive to β2-agonists alone.**

7-Tiotropium may be considered as add-on therapy in patients **whose asthma is not well controlled with a medium-to-high dose of ICS and LABA combination therapy**.

Leukotriene Modifiers

1-**Zafirlukast** and **montelukast** are oral leukotriene receptor antagonists (LTRA) that reduce the proinflammatory and bronchoconstriction effects of leukotriene D4.

2-They are less effective than low-dose ICS, and they are **less effective than LABAs when added to ICS for moderate persistent asthma**.

They are **not used** to treat acute exacerbations and must be taken on a regular basis, even during symptom-free periods.

Thank You