# ASTHMA

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# ASTHMA

## DEFINITION

❑The National Asthma Education and Prevention Program (NAEPP) defines asthma as a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role.

❑In susceptible individuals, inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and coughing.

❑These episodes are usually associated with airflow obstruction that is often reversible either spontaneously or with treatment.

•He inflammation also causes an increase in bronchial hyper responsiveness (BHR) to a variety of stimuli.

# PATHOPHYSIOLOGY

•The major characteristics of asthma include a variable degree of airflow obstruction (related to Bronchospasm, edema, and hyper secretion), BHR, and airway inflammation.

•Inhaled allergens cause an early-phase allergic reaction characterized by activation of cells bearing allergen-specific immunoglobulin E (IgE) antibodies.

- There is rapid activation of airway mast cells and macrophages, Which release proinflammatory mediators such as histamine and eicosanoids that induce contraction of airway smooth muscle, mucus secretion, vasodilation, and exudation of plasma in the airways.

- Plasma protein leakage induces a thickened, engorged, oedematous airway wall and a narrowing of the airway lumen with reduced mucus clearance.

- The late-phase inflammatory reaction occurs 6 to 9 hours after allergen provocation and involves recruitment and activation of Eosinophils, T lymphocytes, basophils, neutrophils, and macrophages.

- Eosinophils migrate to the airways and release inflammatory mediators (leukotrienes and granule proteins), cytotoxic mediators, and cytokines.

- T-lymphocyte activation leads to release of cytokines from type 2 T-helper (TH ) cells that mediate allergic inflammation (interleukin [IL]-4, IL-5, and IL-13). Conversely, type 1 T-helper (TH 21) cells produce IL-2 and interferon-γ that are essential for cellular defense mechanisms.

- Allergic asthmatic inflammation may result from an imbalance between TH1 and TH cells.

- Mast cell degranulation in response to allergens results in release of mediators such as histamine; eosinophil, and neutrophil chemotactic factors; leukotrienes C4, D4, and E; prostaglandins; and platelet-activating factor (PAF).

- Histamine is capable of inducing smooth muscle constriction and bronchospasm and may play a role in mucosal edema and mucus secretion.

- Alveolar macrophages release a number of inflammatory mediators, including PAF and leukotrienes B4, C4, and D.

- Production of neutrophil chemotactic factor and Eosinophils chemo tactic factor furthers the inflammatory process.

- Neutrophils are also a source of mediators (PAFs, prostaglandins, thromboxanes, and leukotrienes) that contribute to BHR and airway inflammation.

- The 5-lipoxygenase pathway of arachidonic acid metabolism is responsible for production of cysteinyl leukotrienes.

- Bronchial epithelial cells participate in inflammation by releasing eicosanoids, peptidases, matrix proteins, cytokines, and nitric oxide. Epithelial shedding results in heightened airway responsiveness, altered permeability of the airway mucosa, depletion of epithelial-derived relaxant factors, and loss of enzymes responsible for degrading inflammatory neuropeptides.

- The exudative inflammatory process and sloughing of epithelial cells into theairway lumen impair mucociliary transport. The bronchial glands are increased in size, and the goblet cells are increased in size and number. Expectorated mucus from patients with asthma tends to have high viscosity.

- The airway is innervated by parasympathetic, sympathetic, and nonadrenergic inhibitory nerves.

- The normal resting tone of airway smooth muscle is maintained by vagal efferent activity, and bronchoconstriction can be mediated by vagal stimulation in the small bronchi.

- Airway smooth muscle contains noninnervated ß – adrenergic receptors that produce bronchodilation.

- The nonadrenergic, noncholinergic nervous system in the trachea and bronchi may amplify inflammation in asthma by releasing nitric oxide.

# CLINICAL PRESENTATION

## CHRONIC ASTHMA

Patients May Also Complain Of Episodes Of

- Dyspnea,
- Chest Tightness,
- Coughing (Particularly At Night),
- Wheezing, Or A Whistling Sound When Breathing.

## SIGNS

- Expiratory Wheezing On Auscultation,
- Dry Hacking Cough, Or Signs Of Atopy (E.G., Allergic Rhinitis Or Eczema).

•Asthma can vary from chronic daily symptoms to only intermittent symptoms.

•The intervals between symptoms may be days, weeks, months, or years.

❑The severity is determined by lung function

➢symptoms Nighttimes Awakenings,

➢ Interference With Normal Activity Prior To Therapy.

Patients can present with mild intermittent symptoms that require no medications or only occasional use of short-acting inhaled ß-agonists to severe chronic asthma symptoms despite receiving multiple medications.

# SEVERE ACUTE ASTHMA

- Uncontrolled asthma can progress to an acute state where inflammation, airway edema, excessive mucus accumulation, and severe bronchospasm result in profound airway narrowing that is poorly responsive to usual bronchodilator therapy.

- Patients may be anxious in acute distress and complain of severe dyspnea, shortness of breath, chest tightness, or burning.

- They may be able to say only a few words with each breath. Symptoms are unresponsive to usual measures.

- Signs include expiratory and Inspiratory wheezing on auscultation, dry hacking cough, tachypnea, tachycardia, pallor or cyanosis, and hyperinflated chest with intercostals and supraclavicular retractions.

- Breath sounds may be diminished with very severe obstruction.

# DIAGNOSIS

## CHRONIC ASTHMA

- Asthma Is Made Primarily By A History Of Recurrent Episodes Of Coughing, Wheezing, Chest Tightness, Or Shortness Of Breath And Confirmatory Spirometry.

- The patient may have a family history of allergy or asthma or have symptoms of allergic rhinitis.

- A history of exercise or cold air precipitating dyspnea or increased symptoms during specific allergen seasons also suggests asthma.

- Spirometry demonstrates obstruction (forced expiratory volume in 1 second [FEV ß 908 21]/forced vital capacity less than 80%) with reversibility after inhaled -agonist administration (at least a 12% improvement in FEV).

- Failure of pulmonary function to improve acutely does not necessarily rule out asthma.

- If baseline Spirometry is normal, challenge testing with exercise, histamine, or methacholine can be used to elicit BHR.

# ACUTE SEVERE ASTHMA

- Peak expiratory flow (PEF) and FEV are less than 50% of normal predicted values. Pulse oximetry reveals decreased arterial oxygen and O2 saturations.

- The best predictor of outcome is early response to treatment as measured by improvement in FEV 1 at 30 minutes after inhaled ß-agonists.

- Arterial blood gases may reveal metabolic acidosis and a low PaO2.

- The history and physical examination should be obtained while initial therapy is being provided.

A history of previous asthma exacerbations

- (e.g., hospitalizations, intubations) and complicating illnesses (e.g., cardiac disease, diabetes) should be obtained.

- The patient should be examined to assess hydration status; use of accessory muscles of respiration; and the presence of cyanosis, pneumonia, pneumothorax, pneumomediastinum, and upper airway obstruction.

- A complete blood count may be appropriate for patients with fever or purulent sputum.

# DESIRED OUTCOME

## CHRONIC ASTHMA

✓ Reducing impairment

(1) prevent chronic and troublesome symptoms (e.g., coughing or breathlessness in the daytime, at night, or after exertion);

(2) require infrequent use **(**=2 days/wk) of inhaled short-acting – agonist for quick relief of symptoms (not including prevention of exercise-induced bronchospasm [EIB]);

(3) maintain (near-) normal pulmonary function;

(4) maintain normal activity levels (including exercise and attendance at work or school);

(5) Meet patients' and families' expectation of and satisfaction with care.

✓ Reducing risk:

(1) prevent recurrent exacerbations and minimize the need for visits or hospitalizations;

(2) prevent loss of lung function; for children, prevent reduced lung growth;

(3) minimal or no adverse effects of therapy.

# ACUTE SEVERE ASTHMA

The goals of treatment include:

(1) correction of significant hypoxemia;

(2) rapid reversal of airway obstruction (within minutes);

(3) reduction of the likelihood of recurrence of severe airflow obstruction; and

(4) development of a written action plan in case of a future exacerbation.

# NONPHARMACOLOGIC THERAPY

- Self-management programs improve adherence to medication regimens, self management skills, and use of healthcare services.

- Objective measurements of airflow obstruction with a home peak flow meter may not necessarily improve patient outcomes.

- The NAEPP advocates use of PEF monitoring only for patients with severe persistent asthma who have difficulty perceiving airway obstruction.

- Avoidance of known allergenic triggers can improve symptoms, reduce medication use, and decrease BHR.

- Environmental triggers (e.g., animals) should be avoided in sensitive patients, and those who smoke should be encouraged to stop.

- Patients with acute severe asthma should receive supplemental oxygen therapy to maintain arterial oxygen saturation above 90% (above 95% in pregnant women and patients with heart disease).

- Significant dehydration should be corrected; urine specific gravity may help guide therapy in young children, in whom assessment of hydration status may be difficult.

# Classifying Asthma Severity & "Step Care"

Persistent Asthma

| | Intermittent | Mild | Moderate | Severe |
|---|---|---|---|---|
| **Symptoms** | ≤2 days/week | ≤2 days/week but not daily | Daily | Throughout the day |
| **Night Awakenings** | ≤2 days/month | 3-4 times/month | >1 time/week but not nightly | Often 7 times/week |
| **Use of SABAs (not for EIB)** | ≤2 days/week | >2 days/week but not daily | Daily | Several times per day |
| **Interference w/ Normal activity** | None | Minor limitation | Some limitation | Extremely limitated |
| **Lung Function** | $FEV_1$>80% predicted<br>$FEV_1$/FVC normal | $FEV_1$≥80% predicted<br>$FEV_1$/FVC normal | $FEV_1$=60-80% predicted<br>$FEV_1$/FVC reduced 5% | $FEV_1$<60% predicted<br>$FEV_1$/FVC reduced >5% |
| **Recommend Step for Initiating Treatment** | Step 1 | Step 2 | Step 3 | Steps 4 - 6 |

asthmaseverity.png

Severity of Symptoms →

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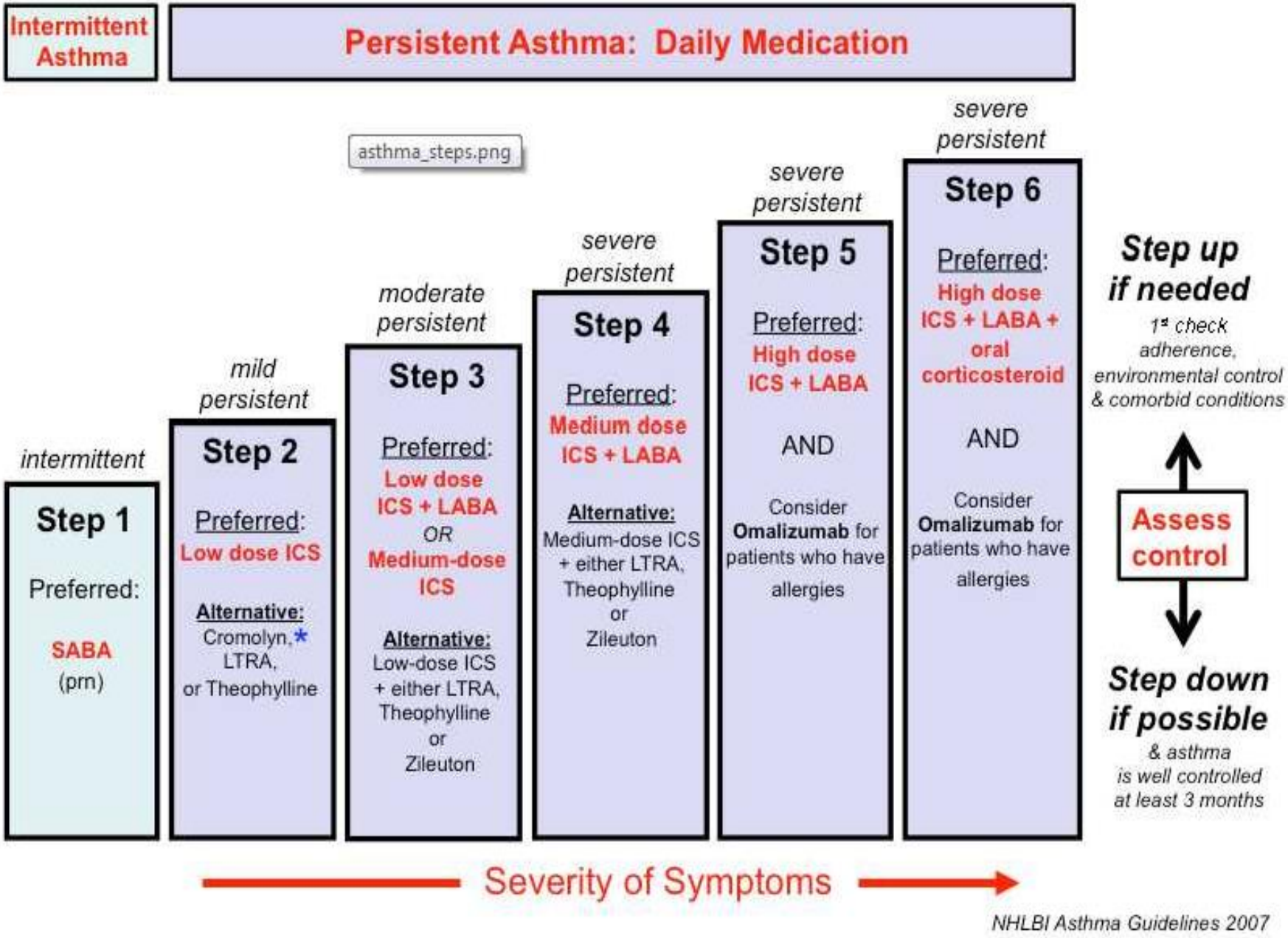
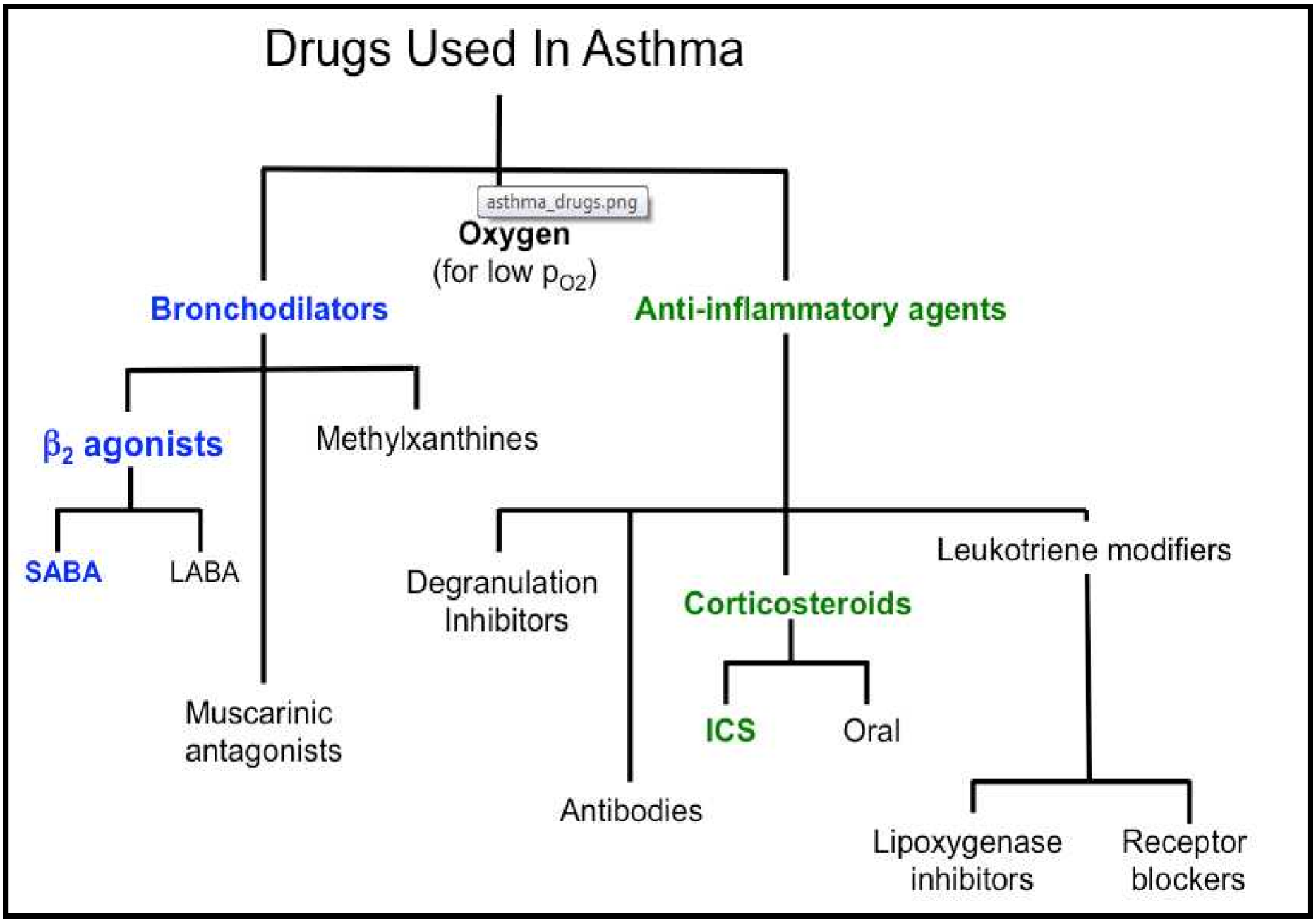
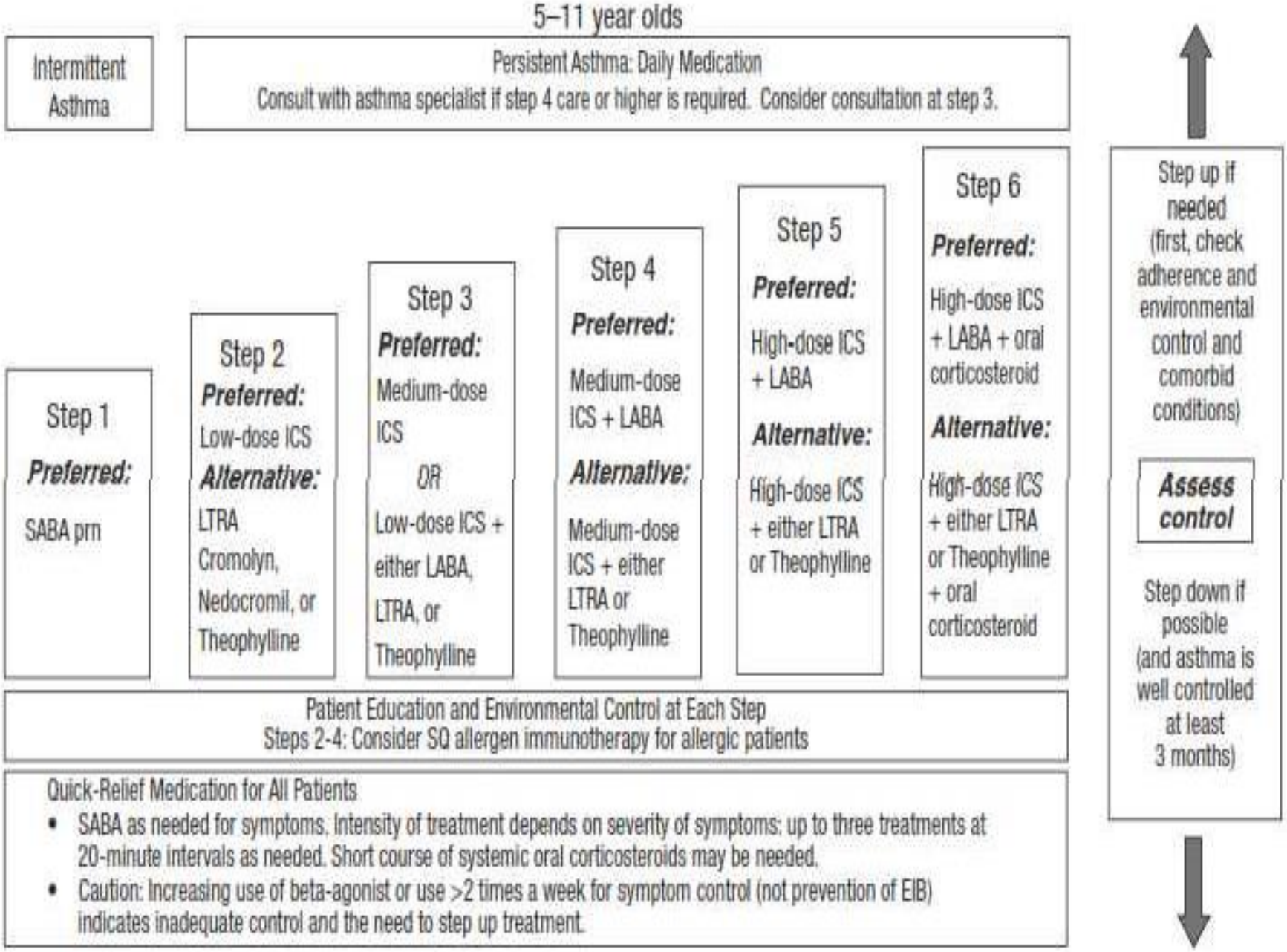
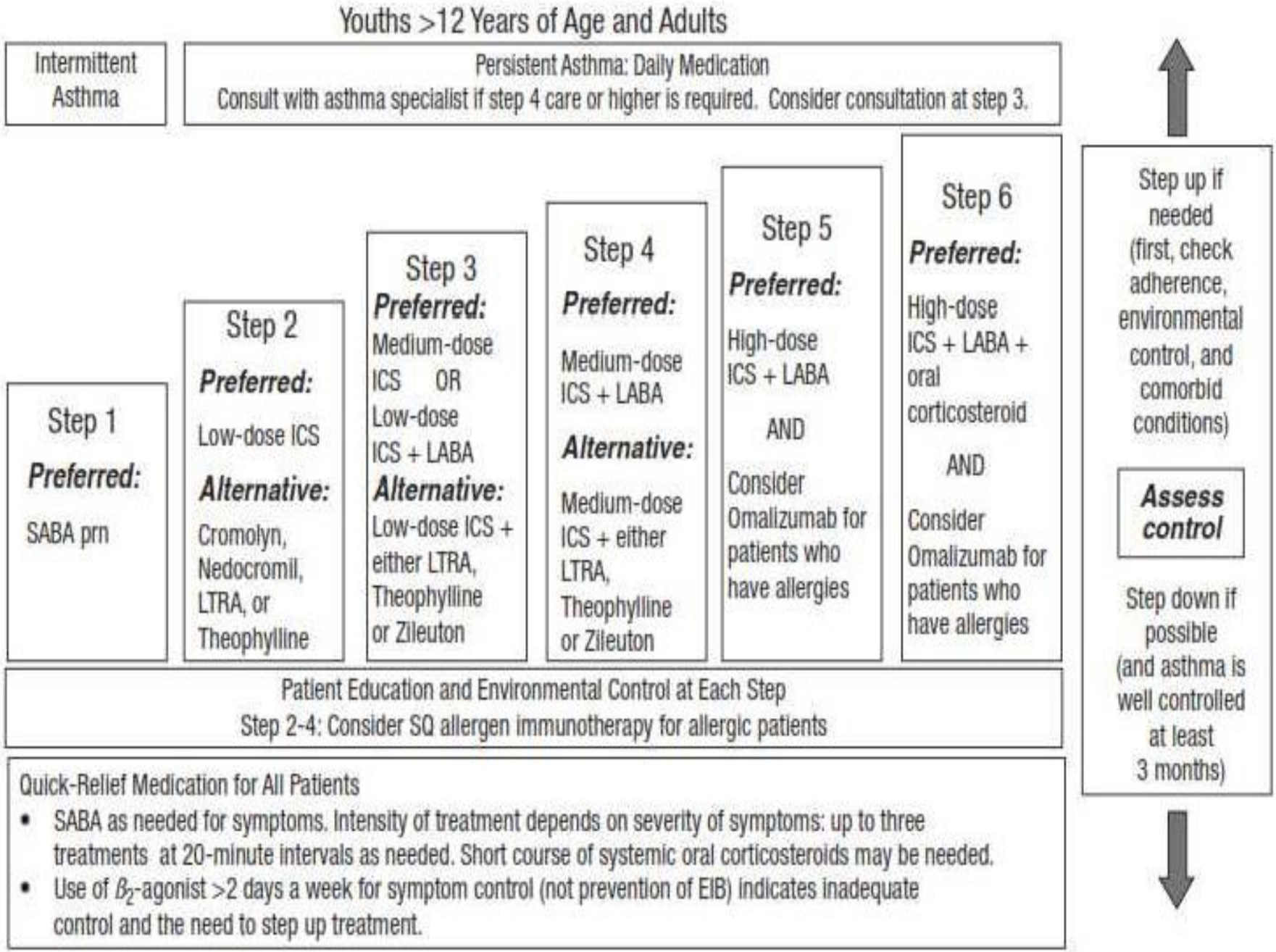
# Stepwise Approach for Managing Asthma in Adults




*NHLBI Asthma Guidelines 2007*


Drugs Used In Asthma
asthma_drugs.png
Oxygen
(for low $p_{O2}$)
Bronchodilators
Anti-inflammatory agents
$\beta_2$ agonists
Methylxanthines
SABA
LABA
Muscarinic antagonists
Degranulation Inhibitors
Corticosteroids
Leukotriene modifiers
ICS
Oral
Antibodies
Lipoxygenase inhibitors
Receptor blockers


5–11 year olds
Intermittent Asthma
Persistent Asthma: Daily Medication
Consult with asthma specialist if step 4 care or higher is required. Consider consultation at step 3.
Step 1
Preferred:
SABA prn
Step 2
Preferred:
Low-dose ICS
Alternative:
LTRA
Cromolyn, Nedocromil, or Theophylline
Step 3
Preferred:
Medium-dose ICS
OR
Low-dose ICS + either LABA, LTRA, or Theophylline
Step 4
Preferred:
Medium-dose ICS + LABA
Alternative:
Medium-dose ICS + either LTRA or Theophylline
Step 5
Preferred:
High-dose ICS + LABA
Alternative:
High-dose ICS + either LTRA or Theophylline
Step 6
Preferred:
High-dose ICS + LABA + oral corticosteroid
Alternative:
High-dose ICS + either LTRA or Theophylline + oral corticosteroid
Step up if needed (first, check adherence and environmental control and comorbid conditions)
Assess control
Step down if possible (and asthma is well controlled at least 3 months)
Patient Education and Environmental Control at Each Step
Steps 2-4: Consider SQ allergen immunotherapy for allergic patients
Quick-Relief Medication for All Patients
• SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to three treatments at 20-minute intervals as needed. Short course of systemic oral corticosteroids may be needed.
• Caution: Increasing use of beta-agonist or use >2 times a week for symptom control (not prevention of EIB) indicates inadequate control and the need to step up treatment.


Youths >12 Years of Age and Adults
Intermittent Asthma
Persistent Asthma: Daily Medication
Consult with asthma specialist if step 4 care or higher is required. Consider consultation at step 3.
Step 1
Preferred:
SABA prn
Step 2
Preferred:
Low-dose ICS
Alternative:
Cromolyn, Nedocromil, LTRA, or Theophylline
Step 3
Preferred:
Medium-dose ICS OR Low-dose ICS + LABA
Alternative:
Low-dose ICS + either LTRA, Theophylline or Zileuton
Step 4
Preferred:
Medium-dose ICS + LABA
Alternative:
Medium-dose ICS + either LTRA, Theophylline or Zileuton
Step 5
Preferred:
High-dose ICS + LABA
AND
Consider Omalizumab for patients who have allergies
Step 6
Preferred:
High-dose ICS + LABA + oral corticosteroid
AND
Consider Omalizumab for patients who have allergies
Step up if needed (first, check adherence, environmental control, and comorbid conditions)
Assess control
Step down if possible (and asthma is well controlled at least 3 months)
Patient Education and Environmental Control at Each Step
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Quick-Relief Medication for All Patients
• SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to three treatments at 20-minute intervals as needed. Short course of systemic oral corticosteroids may be needed.
• Use of $\beta_2$-agonist >2 days a week for symptom control (not prevention of EIB) indicates inadequate control and the need to step up treatment.

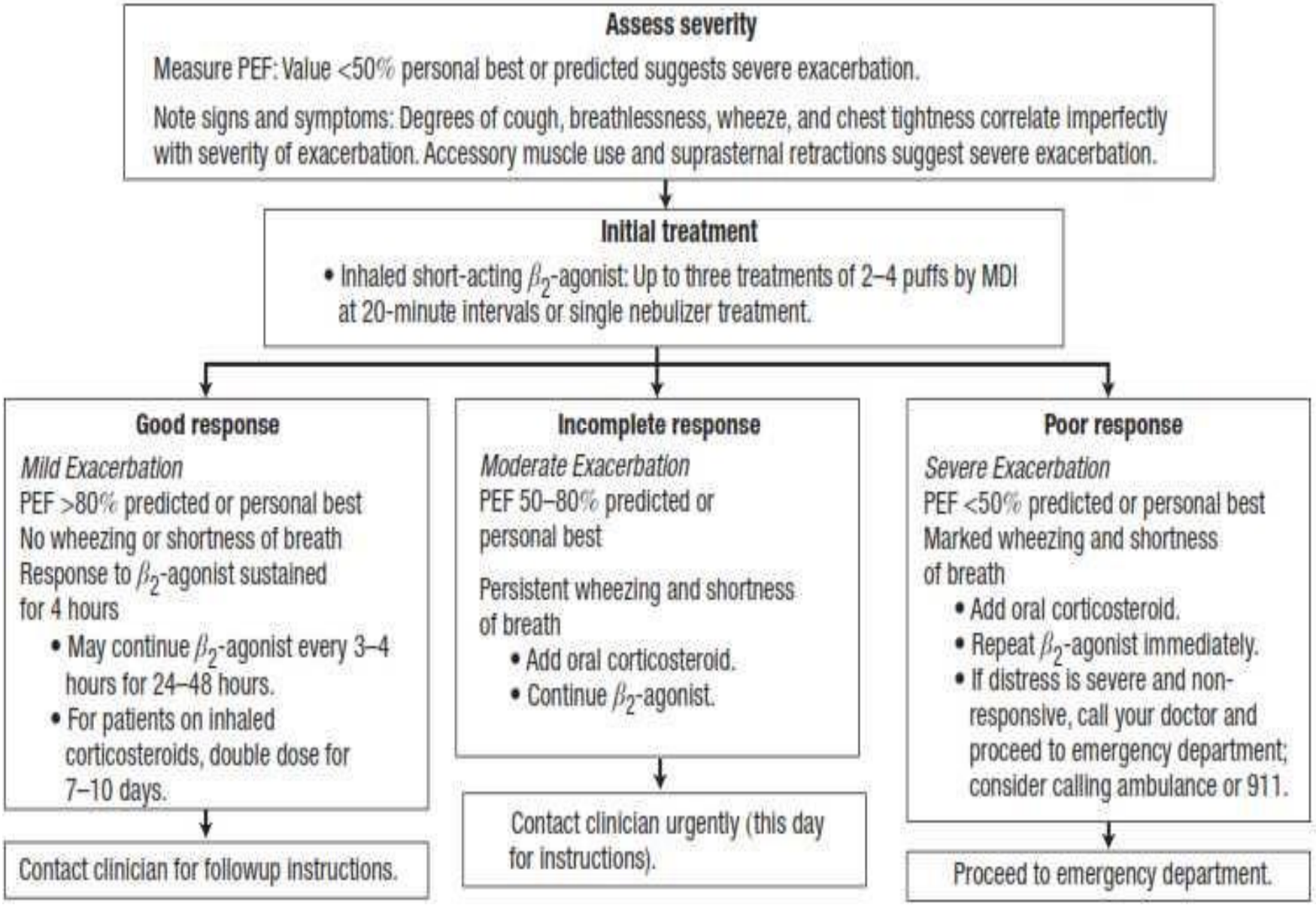
EIB= exercise-induced bronchospasm;

ICS = inhaled corticosteroid;

LABA, long-acting -agonist.

*Adapted from National Institutes of Health, National Heart, Lung, and Blood Institute. National Asthma Education and Prevention Program.*

# Home management of acute asthma exacerbation.



## Long-term asthma control medications

# Inhaled corticosteroids

## These anti-inflammatory drugs include

- fluticasone (Flonase, Flovent HFA),
- budesonide (Pulmicort Flexhaler, Rhinocort),
- flunisolide (Aerospan HFA),
- ciclesonide (Alvesco, Omnaris, Zetonna),
- beclomethasone (Qnasl, Qvar),
- mometasone (Asmanex) and
- fluticasone furoate (Arnuity Ellipta).

# Leukotrienes modifiers

These oral medications — including

- montelukast (Singulair),
- zafirlukast (Accolate) and
- zileuton (Zyflo) — help relieve asthma symptoms for up to 24 hours.

## Long-acting beta agonists

These inhaled medications, which include salmeterol (Serevent) and formoterol (Foradil, Perforomist), open the airways.

## Combination inhalers

These medications — such as

- fluticasone-salmeterol (Advair Diskus),
- budesonide-formoterol (Symbicort) and
- formoterol-mometasone (Dulera) — contain a long-acting beta agonist along with a corticosteroid.

Because these combination inhalers contain long-acting beta agonists, they may increase your risk of having a severe asthma attack.

# Theophylline

Theophylline (Theo-24, Elixophyllin, others) is a daily pill that helps keep the airways open (bronchodilator) by relaxing the muscles around the airways. It's not used as often now as in past years.

# Quick-relief (rescue) medications

are used as needed for rapid, short-term symptom relief during an asthma attack

## ➢Short-acting beta agonists

- These inhaled, quick-relief bronchodilators act within minutes to rapidly ease symptoms during an asthma attack.

They include

- albuterol (ProAir HFA, Ventolin HFA, others) and

- levalbuterol (Xopenex).

# Ipratropium (Atrovent)

Like other bronchodilators, Ipratropium acts quickly to immediately relax your airways, making it easier to breathe. Ipratropium is mostly used for emphysema and chronic bronchitis, but it's sometimes used to treat asthma attacks.

## Oral and intravenous corticosteroids

These medications — which include prednisone and methylprednisolone — relieve airway inflammation caused by severe asthma. They can cause serious side effects when used long term, so they're used only on a short-term basis to treat severe asthma symptoms.

# Allergy medications

## Allergy shots (immunotherapy)

Over time, allergy shots gradually reduce your immune system reaction to specific allergens. You generally receive shots once a week for a few months, then once a month for a period of three to five years.

## Omalizumab (Xolair)

This medication, given as an injection every two to four weeks, is specifically for people who have allergies and severe asthma. It acts by altering the immune system.