PAPH201 | DR. MORA

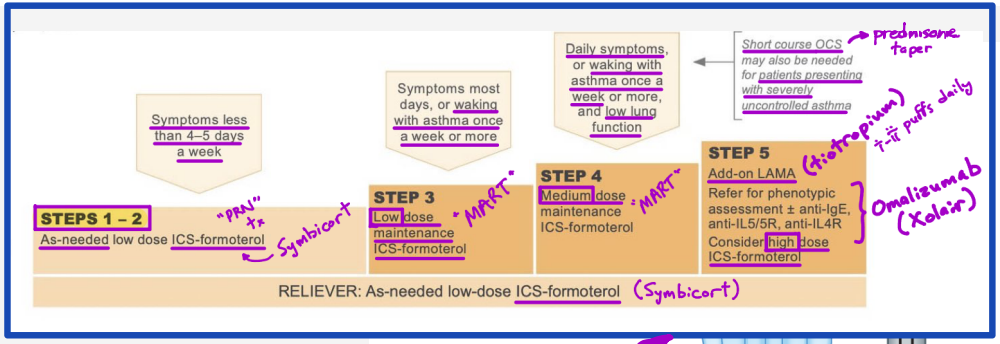
Pulmonary System

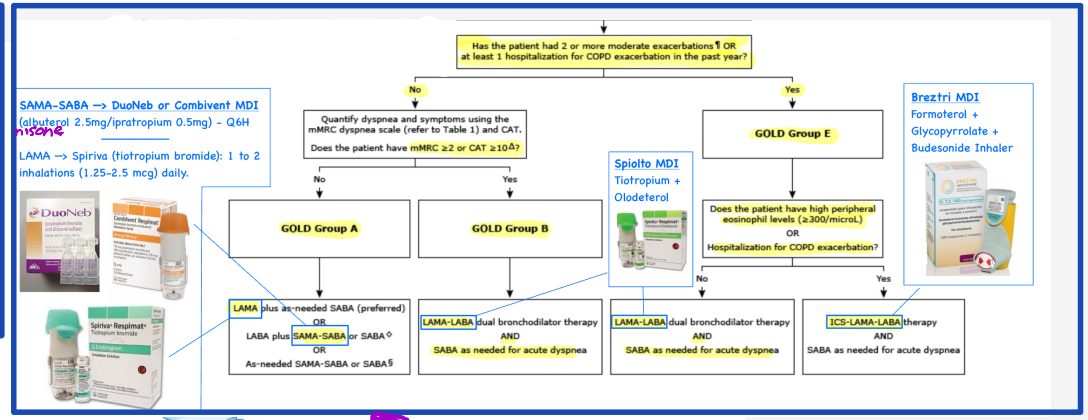
Asthma and COPD Medications

Learning Objectives

Asthma and COPD Medications

1. Classify medications used in COPD and asthma management, including SABA, LABA, anticholinergics, Inhaled Corticosteroids (ICS), and Anticholinergics
2. Describe the mechanisms of action for each drug class, detailing how they alleviate bronchoconstriction, reduce inflammation, and improve airflow
3. Differentiate between rescue and maintenance therapies, identifying which medications are used for acute symptom relief versus long-term control.
4. Recognize common and serious adverse effects of pulmonology medications, including tachycardia, oral thrush, and risk of osteoporosis with long-term corticosteroid use.
5. List contraindications and precautions for each medication class, highlighting patient populations at risk, such as those with cardiac arrhythmias.
6. Evaluate the role of combination therapies, such as LABA/ICS or LABA/LAMA inhalers, and discuss their benefits in reducing exacerbations and improving quality of life.
7. Educate patients on proper inhaler techniques and the importance of medication adherence, addressing common barriers and strategies to improve compliance.





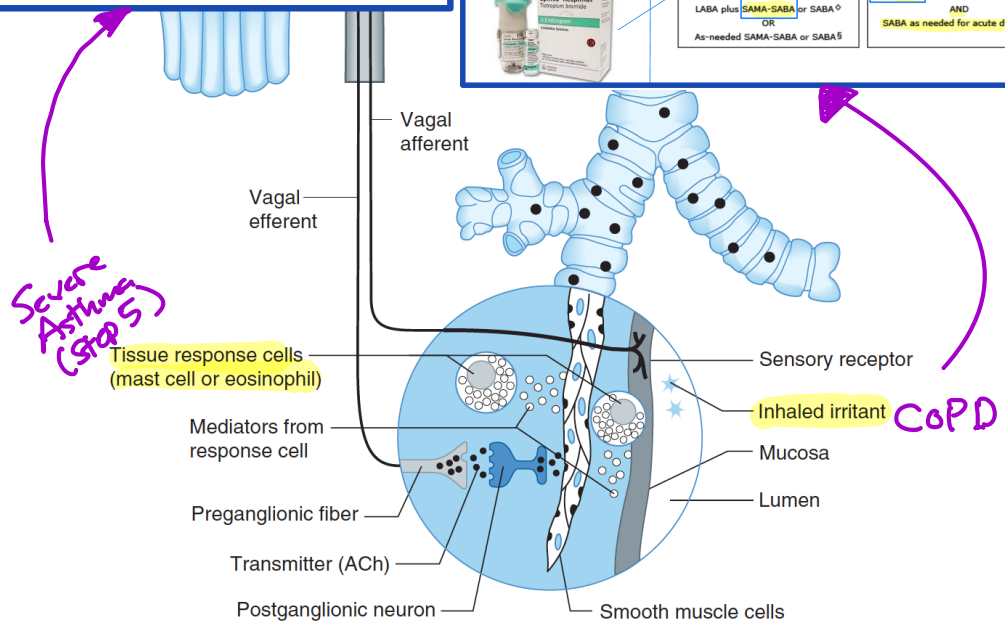
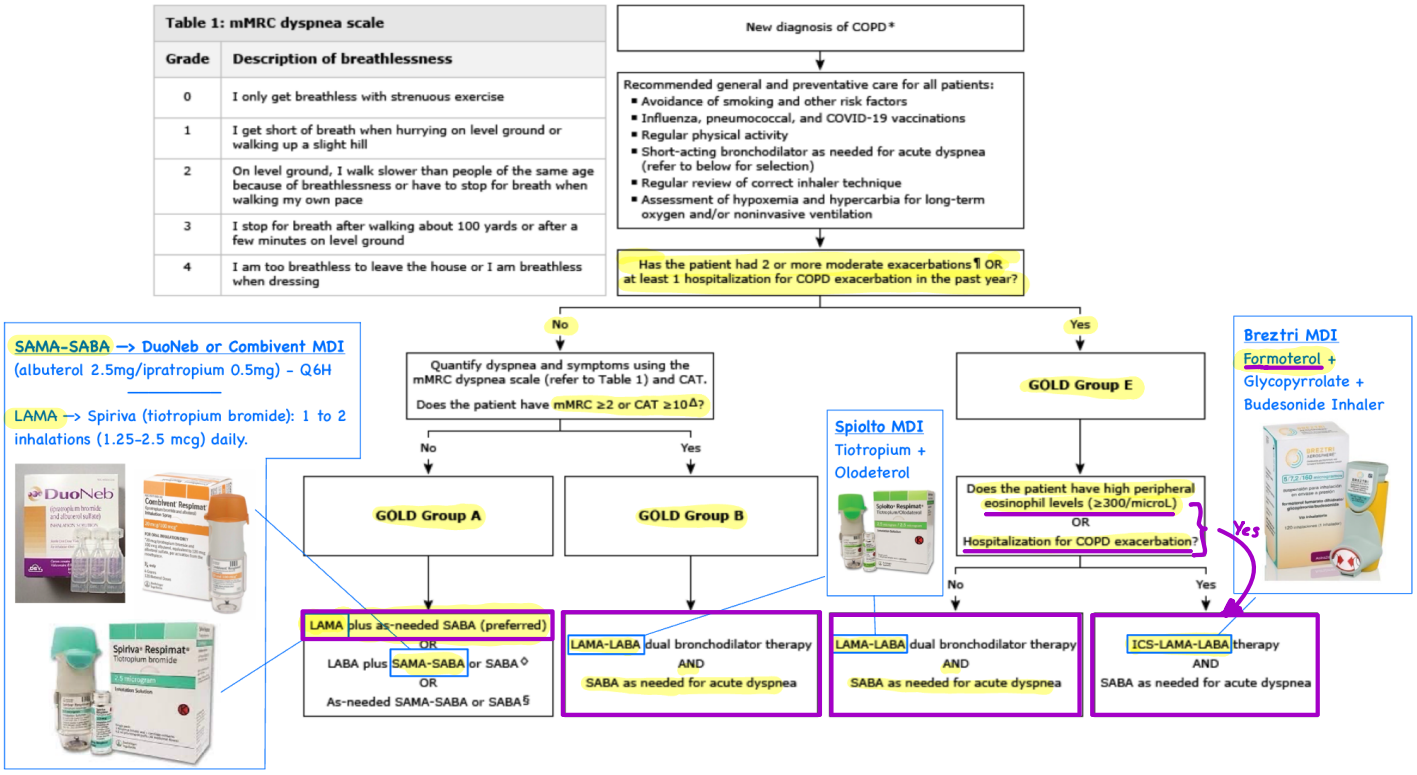


FIGURE 20–6 Mechanisms of response to inhaled irritants. The airway is represented microscopically by a cross section of the wall with branching vagal sensory endings lying adjacent to the lumen. Afferent pathways in the vagus nerves travel to the central nervous system; efferent pathways from the central nervous system travel to efferent ganglia. Postganglionic fibers release acetylcholine (ACh), which binds to muscarinic receptors on airway smooth muscle. Inhaled materials may provoke bronchoconstriction by several possible mechanisms. First, they may trigger the release of chemical mediators from mast cells. Second, they may stimulate afferent receptors to initiate reflex bronchoconstriction or to release tachykinins (eg, substance P) that directly stimulate smooth muscle contraction.

Treatment Algorithm for Newly Diagnosed COPD Patients (UpToDate)

(GOLD: Global Initiative for Chronic Obstructive Lung Disease)

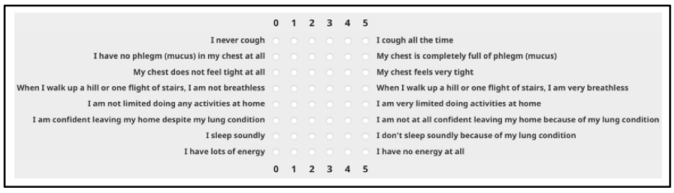
Table 1: mMRC dyspnea scale	
Grade	**Description of breathlessness**
0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on level ground or walking up a slight hill
2	On level ground, I walk slower than people of the same age because of breathlessness or have to stop for breath when walking my own pace
3	I stop for breath after walking about 100 yards or after a few minutes on level ground
4	I am too breathless to leave the house or I am breathless when dressing



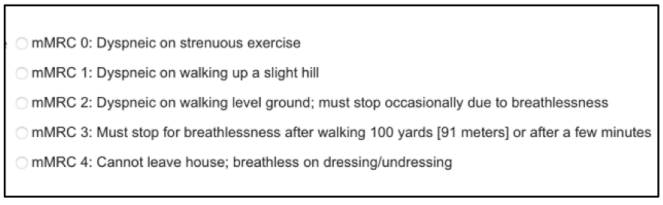
Summary Statements

- COPD is diagnosed based on the presence of chronic resp symptoms (dyspnea, cough, sputum production) accompanied by airflow limitation → severity of symptoms quantified with mMRC dyspnea scale and CAT (COPD Assessment Test) → graded scores determine the most effective treatment approaches for COPD (GOLD Tx Approach).
- The mainstay of drug treatment for stable COPD are inhaled bronchodilators: beta-2 agonists and muscarinic antagonists → commonly given in combination +/- inhaled corticosteroids (ICS).
- GOLD approach focuses on targeting therapies based on symptoms and exacerbation risk (A, B, E groups).

Modified Medical Research Council (mMRC) Scale for Dyspnea



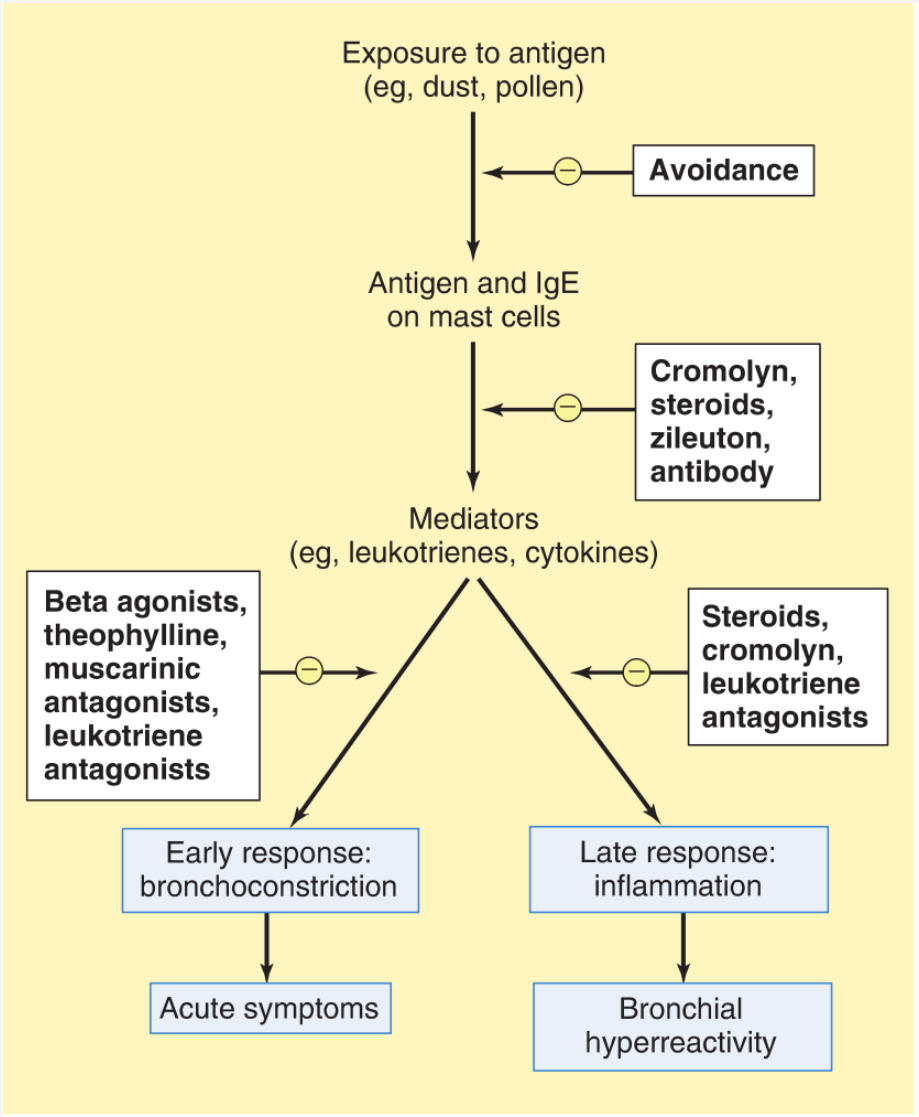
COPD Assessment Test (CAT)

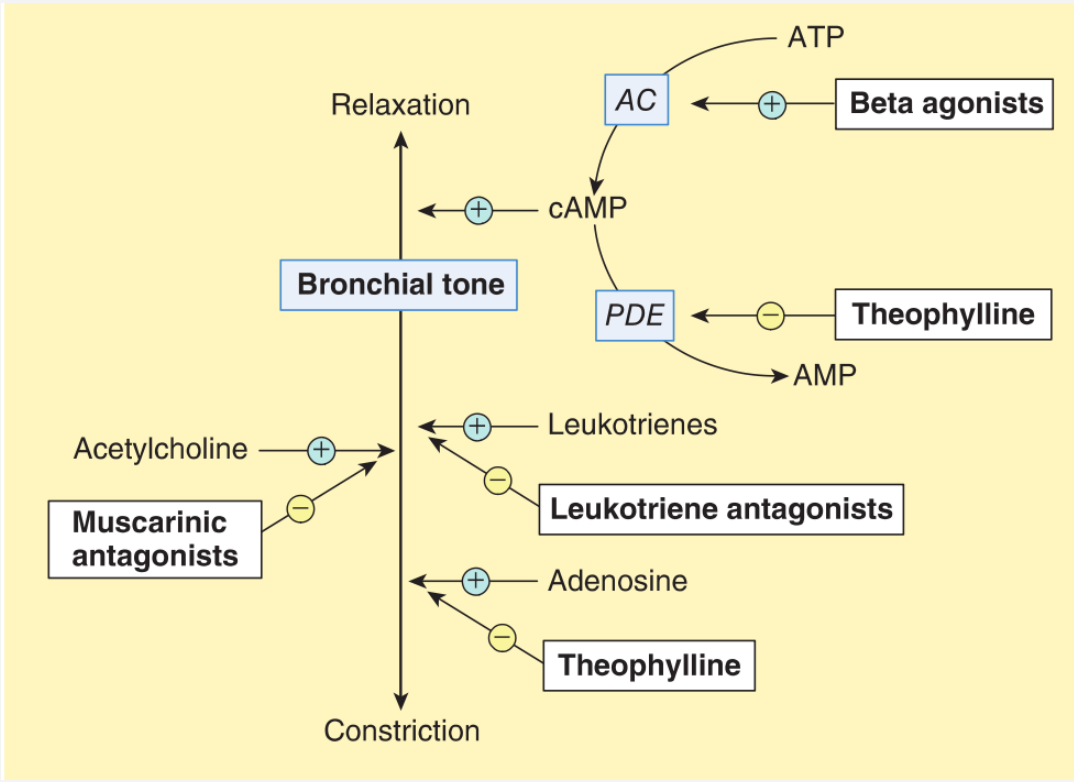


- All COPD patients should be prescribed a SABA for relief of dyspnea and treatment of exacerbations, instead of SAMA → SAMA is not recommended in patients using a LAMA.
- In patients who are taking LABAs without LAMA coadministration, we prefer using SABA-SAMA (e.g., DuoNeb) → dual therapy offers greater bronchodilator response than either agent alone.
- For patients prescribed a LAMA, a SAMA should not be prescribed concomitantly due to cumulative anticholinergic side effects and theoretical blockage of LAMA effects by the SAMA. Patients taking a LAMA should use a SABA alone for relief of dyspnea.

LABA + DuoNeb

LAMA + SABA


Exposure to antigen
(eg, dust, pollen)
Avoidance
Antigen and IgE
on mast cells
Cromolyn,
steroids,
zileuton,
antibody
Mediators
(eg, leukotrienes, cytokines)
Beta agonists,
theophylline,
muscarinic
antagonists,
leukotriene
antagonists
Steroids,
cromolyn,
leukotriene
antagonists
Early response:
bronchoconstriction
Late response:
inflammation
Acute symptoms
Bronchial
hyperreactivity


ATP
AC
Beta agonists
Relaxation
cAMP
Bronchial tone
PDE
Theophylline
AMP
Leukotrienes
Acetylcholine
Leukotriene antagonists
Muscarinic
antagonists
Adenosine
Theophylline
Constriction

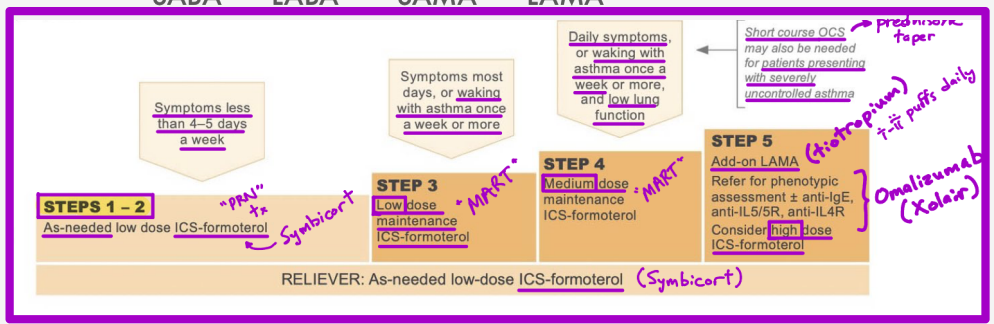
Overview of Condition Management

Asthma

Symbicort (formoterol + budesonide)

Asthma Medications

- Bronchodilators
  - Beta2-agonists
    - SABA
    - LABA
  - Muscarinic antagonists
    - SAMA
    - LAMA
  - Methylxanthines
- Oxygen
- Anti-Inflammatory Agents
  - Corticosteroids
    - ICS
    - Systemic
  - Leukotriene Antagonists
  - Degranulation Inhibitors



Asthma symptoms	Preferred treatment		Alternative treatment	
	Controller	Reliever	Controller	Reliever
Less than twice a month	Low-dose ICS-*formoterol* as needed		Use ICS whenever SABA is needed	SABA as needed
More than twice a month, but less than 4 to 5 days per week	Low-dose ICS-*formoterol* as needed		Low-dose maintenance ICS	SABA as needed
Most days of the week or awakening due to asthma at least once a week	Low-dose maintenance ICS-*formoterol*	Low-dose ICS-*formoterol* as needed	Low-dose maintenance ICS-LABA	SABA as needed
Daily symptoms or awakening due to asthma at least once a week; low lung function	Medium-dose maintenance ICS-*formoterol*	Low-dose ICS-*formoterol* as needed	Medium- or high-dose maintenance ICS-LABA	SABA as needed

Overview of Condition Management

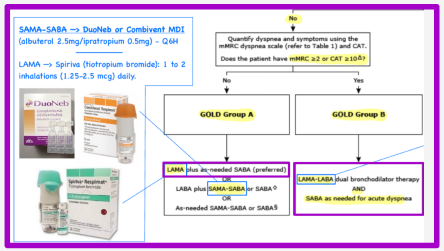
COPD

SABA prn dyspnea

LAMA

COPD Medications

- Bronchodilators
  - Beta2-agonists
    - SABA
    - LABA
  - Muscarinic antagonists
    - SAMA
    - LAMA
  - Methylxanthines
- Oxygen
- Anti-Inflammatory Agents
  - Corticosteroids
    - ICS
    - Systemic
  - PDE-4 inhibitor



GOLD Grp E

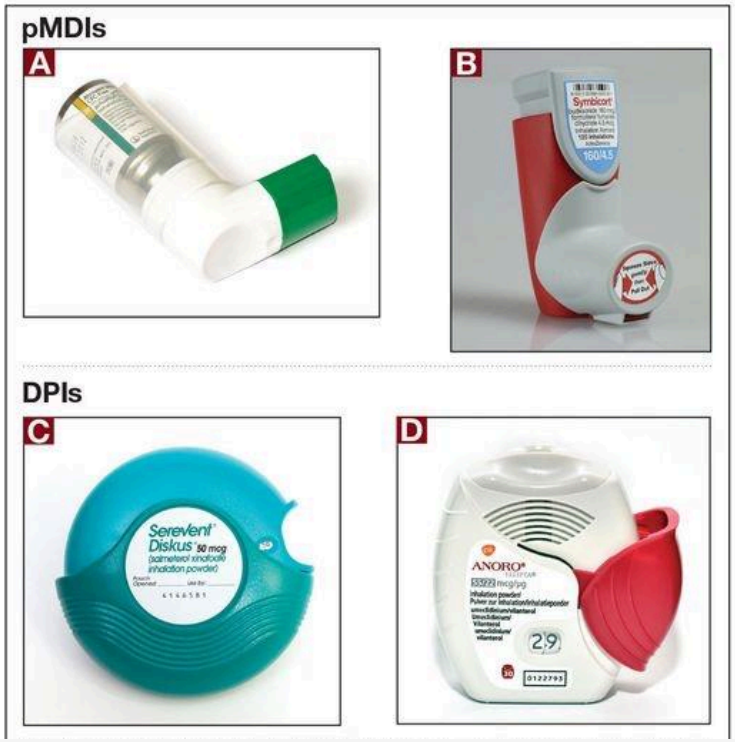
Does the patient have high peripheral eosinophil levels (≥300/microL)
OR
Hospitalization for COPD exacerbation?

Yes

+ SABA (albuterol) prn acute dyspnea

Formulations

Methods for Inhalation of Asthma, COPD Medications

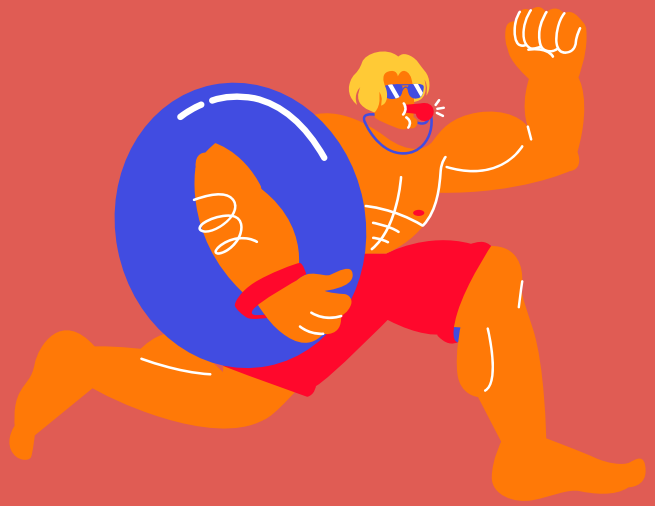


A, B) Metered Dose Inhalers (MDI) use a metered valve to deliver a specific amount of drug to the lungs in the form of a short burst of aerosolized medication during each actuation

C, D) Dry Powder Inhalers (DPI) are breath-actuated, with the patient providing the force necessary to deliver the drug on inhalation;

E) Nebulizers use oxygen, compressed air, or ultrasonic power to convert solutions into small liquid aerosol droplets that can be inhaled into the mouth or nosepiece of the device.

Short Acting Beta Agonist (SABA)



Short-Acting Beta-2 Agonists (SABAs)

Albuterol[A,C], Levalbuterol[A,C]

Formulations

- MDI, inhalation solutions, oral tablets
- Onset: 5-15min
- Duration: 2-4h

Inhaled Beta-2 Agonists

- Levalbuterol (Xopenex)
  - Levalbuterol at ~~hone~~ half the mcg dose produces clinically comparable bronchodilation as albuterol → reduces cardiac adverse effects (tachycardia) and is preferred in patients with atrial fibrillation.

	BETA-1	BETA-2
ALBUTEROL	+	++++
LEVALBUTEROL (Xopenex)	+ / -	++++

SABA
SHORT-ACTING BETA-2 AGONIST

ProAir HFA 4+
METERED DOSE G AG
(200 inhalations)
Albuterol

ProAir RespiClick 4+
DRY POWDER
(200 inhalations)
Albuterol

Proventil HFA 4+
METERED DOSE G AG
(200 inhalations)
Albuterol

Ventolin HFA 4+
METERED DOSE AG
(200 inhalations)
Albuterol

Xopenex HFA 4+
METERED DOSE AG
(200 inhalations)
Levalbuterol

Age (years) approved for asthma
Age (years) approved for bronchospasm
C Approved for COPD

AG Authorized generic available
G AB-rated generics available
(including branded generics)

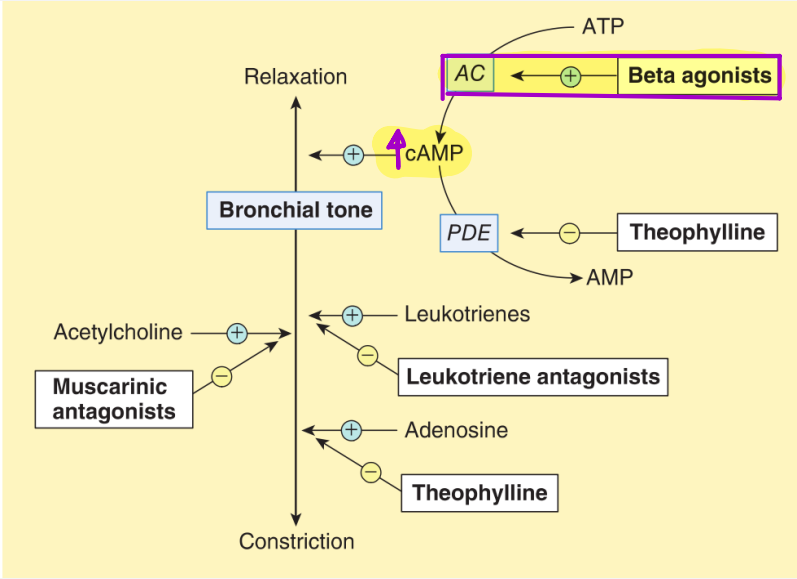
Note: SABAs are FDA-approved for bronchospasm in reversible obstructive airway diseases **and** exercise-induced bronchospasm (EIB), except Xopenex (levalbuterol), which is not indicated for EIB; Airsupra (albuterol/budesonide) is indicated as needed for bronchoconstriction and to reduce the risk of asthma exacerbations; Serevent Diskus (salmeterol) is indicated for EIB, asthma (**in addition to an ICS**), and COPD. Indications and evidence are subject to change and geographic variability.

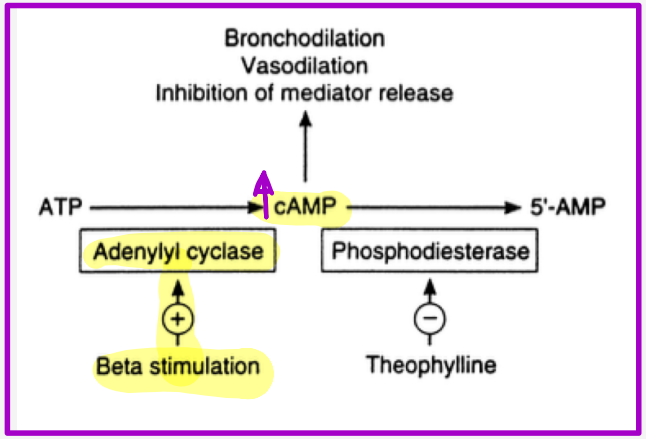
Short-Acting Beta-2 Agonists (SABAs)

Albuterol[A,C], Levalbuterol[A,C]

Mechanism of Action

- Bind β2-adrenergic receptors → conversion of ATP to cAMP → bronchial smooth muscle relaxation → bronchodilation





Short-Acting Beta-2 Agonists (SABAs)

Albuterol[A,C], Levalbuterol[A,C]

Indication

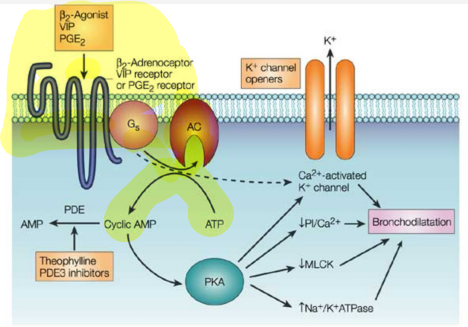
- Acute asthma exacerbations
- Acute bronchospasm in COPD
- Prophylaxis for exercise-induced asthma
- Hyperkalemia
- Not to be used as routine asthma maintenance therapy

GINA Track 2: Asthma — ICS + SABA prn dyspnea

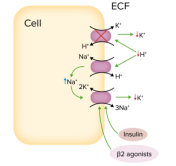
COPD — LAMA + SABA prn dyspnea

Inhaled Beta-2 Agonists

- Mechanism of Action:
  Beta-2 agonists stimulate adenylyl cyclase (AC)
  → converts ATP to cAMP
  → stimulates protein kinase A
  → bronchodilation
- Side Effects: tachycardia, tremors, anxiety, hypokalemia
  Note: all "selective" beta-2 agonists will exert beta-1 agonist effects when used in higher doses



- Albuterol 10-15 mg HHN is indicated for treatment of hyperkalemia
  → beta-2 stimulation (skeletal muscle) → increases cAMP
  → stimulates Na^+/K^+ pump
  → actively transports and shifts K+ intracellular
  → decreases serum K^+



- Regular use of SABA for 1-2 weeks is associated with the following risks:
  (1) increased airway hyperresponsiveness
  (2) reduced bronchodilator efficacy
  (3) increased eosinophils → inflammation
  (4) SABA overuse increases asthma exacerbations → increases risk of mortality

Short-Acting Beta-2 Agonists (SABAs)

Albuterol[A,C], Levalbuterol[A,C]

Sympathomimetic Effects

Adverse Effects

- Tachycardia
  (nonselective β-blockers > β2-selective)
- Tremor
- Hypokalemia
- Nervousness

Contraindications

- Hypersensitivity
- ⚠ Caution in patients with arrhythmias, digoxin use, QT prolonging medications
- Beta-blockers may counteract their effects

Long Acting Beta-Agonist (LABA)

Long-Acting Beta-2 Agonists (LABAs)

Salmeterol[AC], Formoterol[AC], Arformoterol[C], Indacaterol[C], Olodaterol[C], Viltanterol[AC]

Formulations

- DPI, inhaled solution
- Onset:
  - 5min (Formoterol)
  - 30min (Salmeterol)
- Duration: 4h to 12+ hours

Symbicort (preferred)

Advair

LABA
LONG-ACTING BETA-2 AGONIST

Serevent Diskus 4+ 4+ C
DRY POWDER
(60 inhalations)
Salmeterol

Striverdi Respimat C
SOFT MIST
(60 inhalations)
Olodaterol

Age (years) approved for asthma
Age (years) approved for bronchospasm
C Approved for COPD

AG Authorized generic available
G AB-rated generics available
(including branded generics)

Note: SABAs are FDA-approved for bronchospasm in reversible obstructive airway diseases **and** exercise-induced bronchospasm (EIB), except Xopenex (levalbuterol), which is not indicated for EIB; Airsupra (albuterol/budesonide) is indicated as needed for bronchoconstriction and to reduce the risk of asthma exacerbations; Serevent Diskus (salmeterol) is indicated for EIB, asthma (**in addition to an ICS**), and COPD. Indications and evidence are subject to change and geographic variability.

Long-Acting Beta-2 Agonists (LABAs)

Salmeterol[AC], Formoterol[AC], Arformoterol[C], Indacaterol[C], Olodaterol[C], Viltanterol[AC]

Mechanism of Action

- Stimulate β2-adrenergic receptors → prolonged bronchial smooth muscle relaxation → sustained bronchodilation
- Inhibit release of hypersensitivity mediators

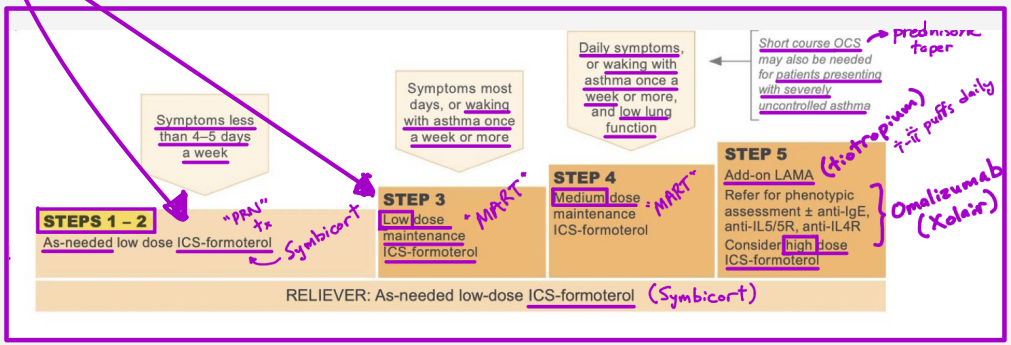
Long-Acting Beta-2 Agonists (LABAs)

Salmeterol[AC], Formoterol[AC], Arformoterol[C], Indacaterol[C], Olodaterol[C], Viltanterol[AC]

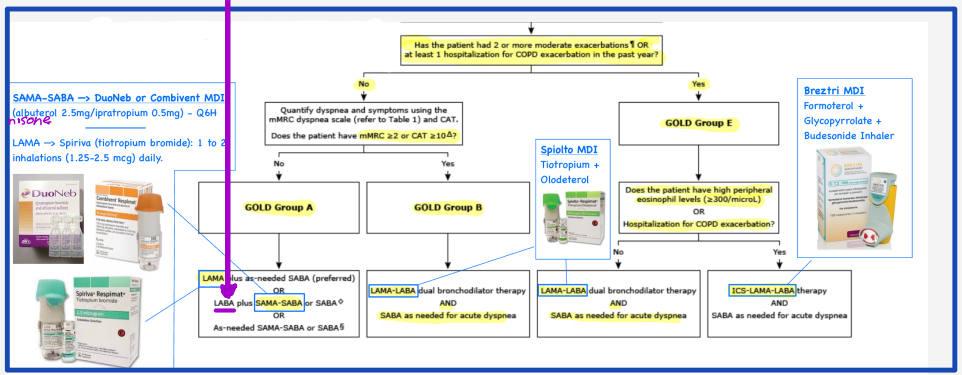
Indication

- Asthma control (use with ICS)
- COPD maintenance therapy

Asthma



COPD



Long-Acting Beta-2 Agonists (LABAs)

Salmeterol[AC], Formoterol[AC], Arformoterol[C], Indacaterol[C], Olodaterol[C], Viltanterol[AC]

Adverse Effects

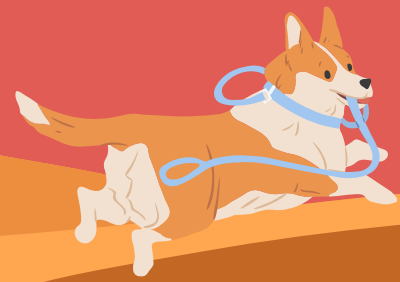
- Tachycardia
- Muscle cramps
- Headache
- Paradoxical bronchospasm

Contraindications

- Monotherapy in asthma (without ICS)
- Hypersensitivity
- Milk allergy (salmeterol, vilanterol)
- Cautions similar to SABAs

DPI (dry powder inhalers) contain lactose. (Advair)

Anticholinergics



Anticholinergics

Ipratropium[C], Tiotropium[C], Umeclidinium[C]

Formulations

- DPI, MDI, Inhaled solution
- Ipratropium – short acting
- Tiotropium – longer acting

SAMA
SHORT-ACTING MUSCARINIC ANTAGONIST

Atrovent HFA C
METERED DOSE
(200 inhalations)
Ipratropium

LAMA
LONG-ACTING MUSCARINIC ANTAGONIST

Incruse Ellipta C
DRY POWDER
(30 inhalations)
Umeclidinium

Spiriva HandiHaler C G
DRY POWDER
(30 doses [2 inhalations/capsule])
Tiotropium

Spiriva Respimat 6+ C
SOFT MIST
(60 inhalations)
Tiotropium

Tudorza Pressair C
DRY POWDER
(60 inhalations)
Aclidinium

Age (years) approved for asthma
Age (years) approved for bronchospasm
C Approved for COPD

AG **Authorized generic available**
G **AB-rated generics available**
(including branded generics)

Note: SABAs are FDA-approved for bronchospasm in reversible obstructive airway diseases **and** exercise-induced bronchospasm (EIB), except Xopenex (levalbuterol), which is not indicated for EIB; Airsupra (albuterol/budesonide) is indicated as needed for bronchoconstriction and to reduce the risk of asthma exacerbations; Serevent Diskus (salmeterol) is indicated for EIB, asthma (**in addition to an ICS**), and COPD. Indications and evidence are subject to change and geographic variability.

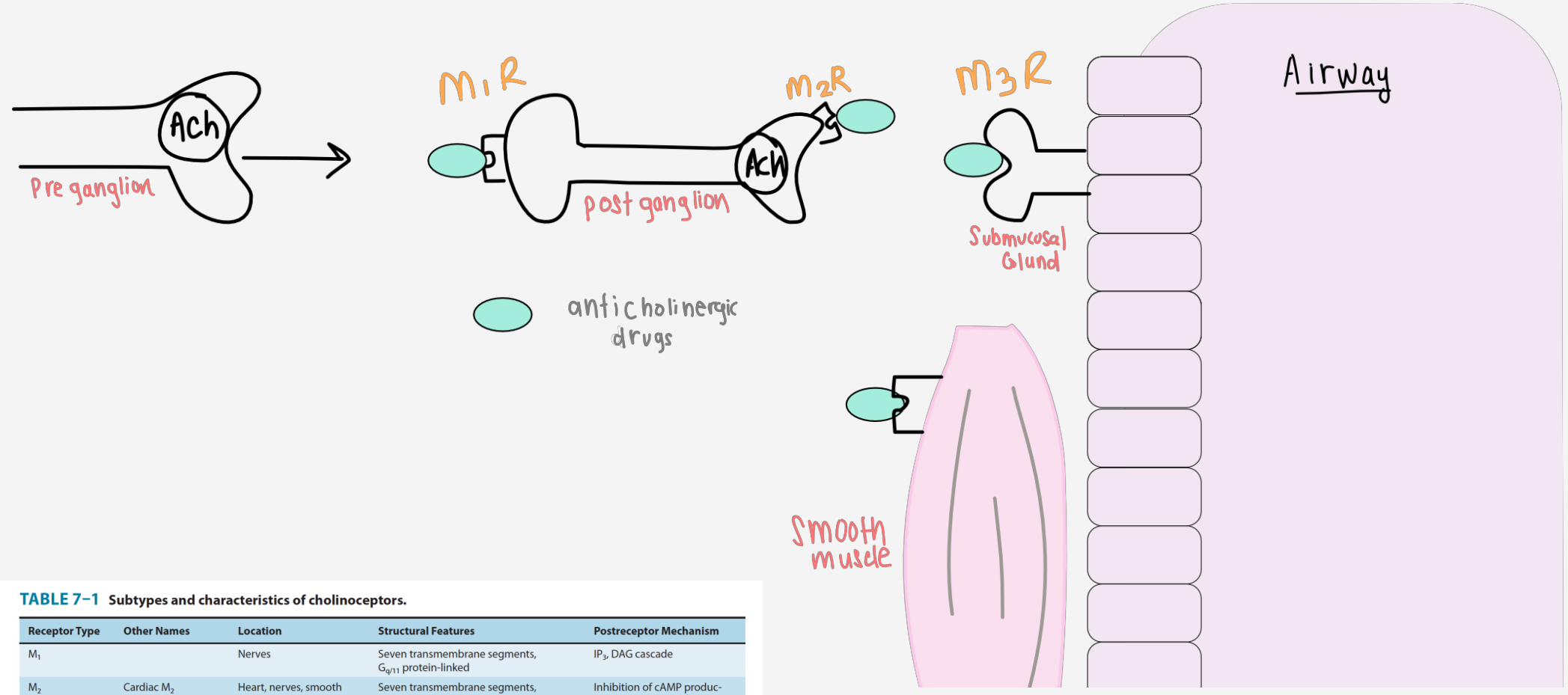


TABLE 7–1 Subtypes and characteristics of cholinoceptors.

Receptor Type	Other Names	Location	Structural Features	Postreceptor Mechanism
M_1		Nerves	Seven transmembrane segments, $G_{q/11}$ protein-linked	IP_3, DAG cascade
M_2	Cardiac M_2	Heart, nerves, smooth muscle	Seven transmembrane segments, $G_{i/o}$ protein-linked	Inhibition of cAMP production, activation of K^+ channels
M_3		Glands, smooth muscle, endothelium	Seven transmembrane segments, $G_{q/11}$ protein-linked	IP_3, DAG cascade
M_4		CNS	Seven transmembrane segments, $G_{i/o}$ protein-linked	Inhibition of cAMP production
M_5		CNS	Seven transmembrane segments, $G_{q/11}$ protein-linked	IP_3, DAG cascade
N_M	Muscle type, end plate receptor	Skeletal muscle neuromuscular junction	Pentamer[1] $[(\alpha1)_2\beta1\delta\gamma)]$	Na^+, K^+ depolarizing ion channel
N_N	Neuronal type, ganglion receptor	CNS, postganglionic cell body, dendrites	Pentamer[1] with α and β subunits only, eg, $(\alpha4)_2(\beta2)_3$ (CNS) or $\alpha3\alpha5(\beta2)_3$ (ganglia)	Na^+, K^+ depolarizing ion channel

Anticholinergics

Ipratropium^{C}, Tiotropium^{C}, Umeclidinium^{C}

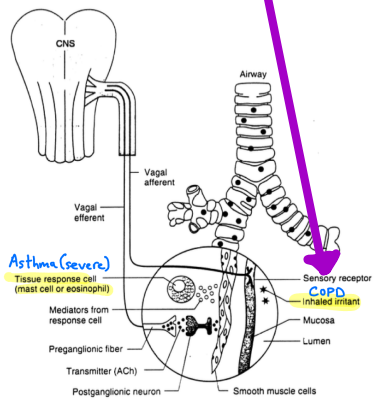
Mechanism of Action

- Irritants stimulate upper airway mucosa → ⊕ vagus nerve release of acetylcholine → ⊕ pulmonary secretions
- Block muscarinic (M_1, M_2, M_3) receptors → inhibit Ach-mediated bronchoconstriction & mucus production

Inhaled Anti-Cholinergic (Anti-Muscarinic) Agents (SAMA & LAMA)

SAMA: Ipratropium Bromide (Atrovent)
LAMA: Tiotropium Bromide (Spiriva)

- MOA: (1) inhibit muscarinic cholinergic receptors → bronchodilation, and (2) reduce intrinsic vagal tone of the airways → block reflex bronchoconstriction secondary to irritants or to GERD
- These agents are more effective in COPD, in which vagal-mediated bronchoconstriction is predominant, than in asthma
- Since SAMA and LAMA are less effective than beta-2 agonists in treatment of asthma/COPD, they are usually combined with beta-2 agonists: DuoNeb (albuterol 2.5 mg / ipratropium 0.5 mg in 3 ml saline)
- Side Effects: systemic anticholinergic effects include dry mouth, blurred vision, urinary retention, etc…



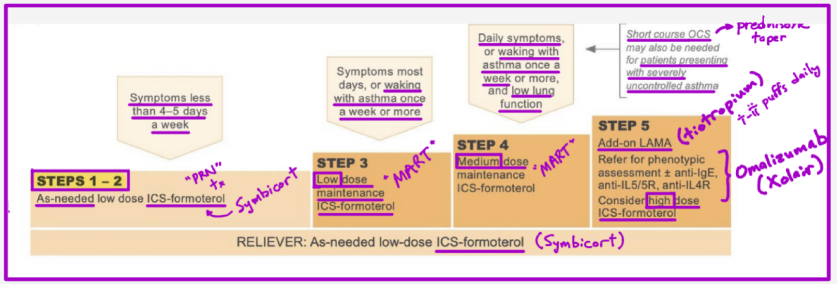
Anticholinergics

Ipratropium[C], Tiotropium[C], Umeclidinium[C]

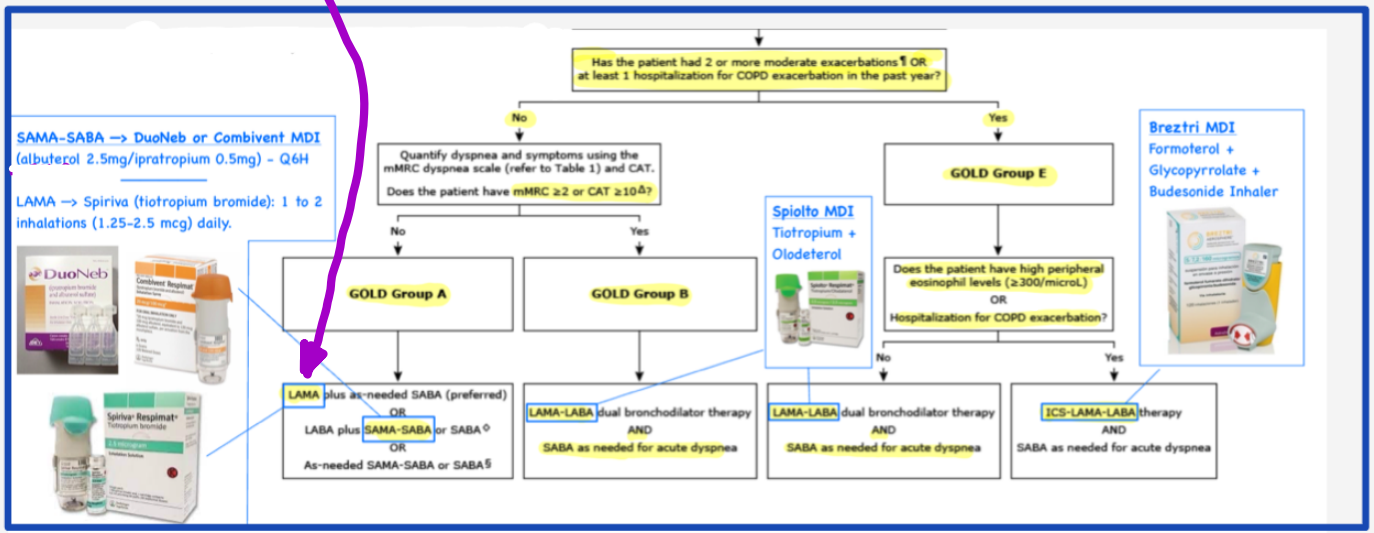
Indication

- Bronchospasms in COPD
- Asthma (off-label)
  - ↳ add on LAMA in step 5 (GINA)

Asthma



COPD



Anticholinergics

Ipratropium[C], Tiotropium[C], Umeclidinium[C]

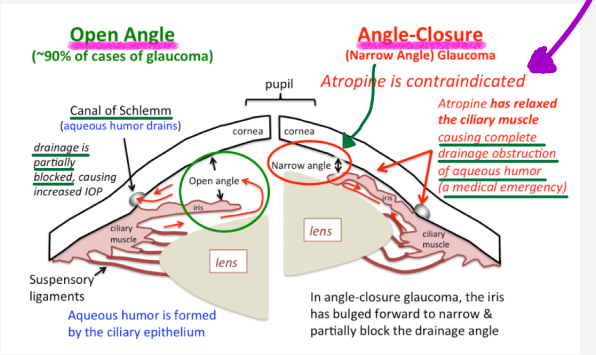
Adverse Effects

- Dry mouth
- Cough
- Bitter taste
- Urinary retention

anti-ACh SEs

Contraindications

- Hypersensitivity to atropine derivatives
- Narrow angle glaucoma
- Prostatic hypertrophy



Methylxanthines

Methylxanthines

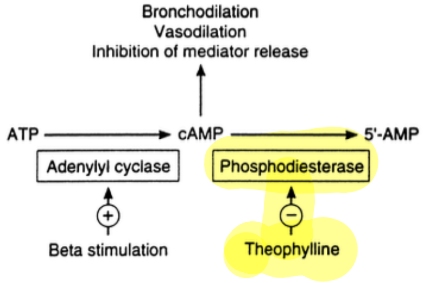
Theophylline[A,C]

Formulations

- Oral tablet, liquid, intravenous

Methylxanthine: Theophylline (Theo-Dur)

- General Considerations
  - Theophylline is not effective as an aerosolized inhaler and must be given orally or intravenously → increases systemic side effects.
  - Theophylline is less effective as a bronchodilator than beta-2 inhaled agonists.
  - Theophylline causes many drug-drug interactions and serious adverse effects.
  - Theophylline has a narrow therapeutic range (10-20 mcg/ml) → potentiates toxicities.
  - Theophylline is considered a 3rd or 4th line adjunctive agent in persistent asthma.
- Mechanisms of Action: Besides smooth muscle relaxation, the beneficial effects of theophylline that have been postulated have included an anti-inflammatory effect, an improvement in mucociliary clearance, increased diaphragmatic contractility, and increased respiratory drive.
- Side Effects & Toxicities: nausea, vomiting, dyspepsia, GI reflux, diarrhea, tachycardia, insomnia, headaches, irritability, arrhythmias, seizures, cardiac arrest, death.



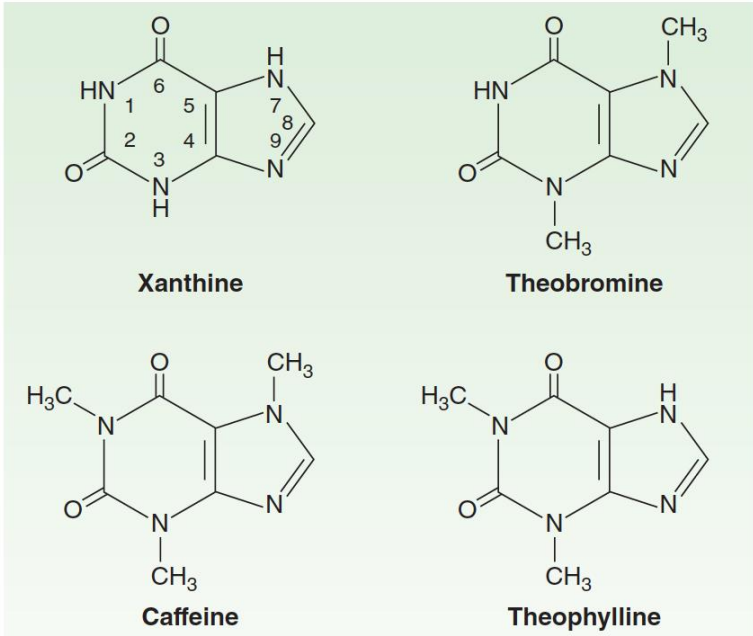
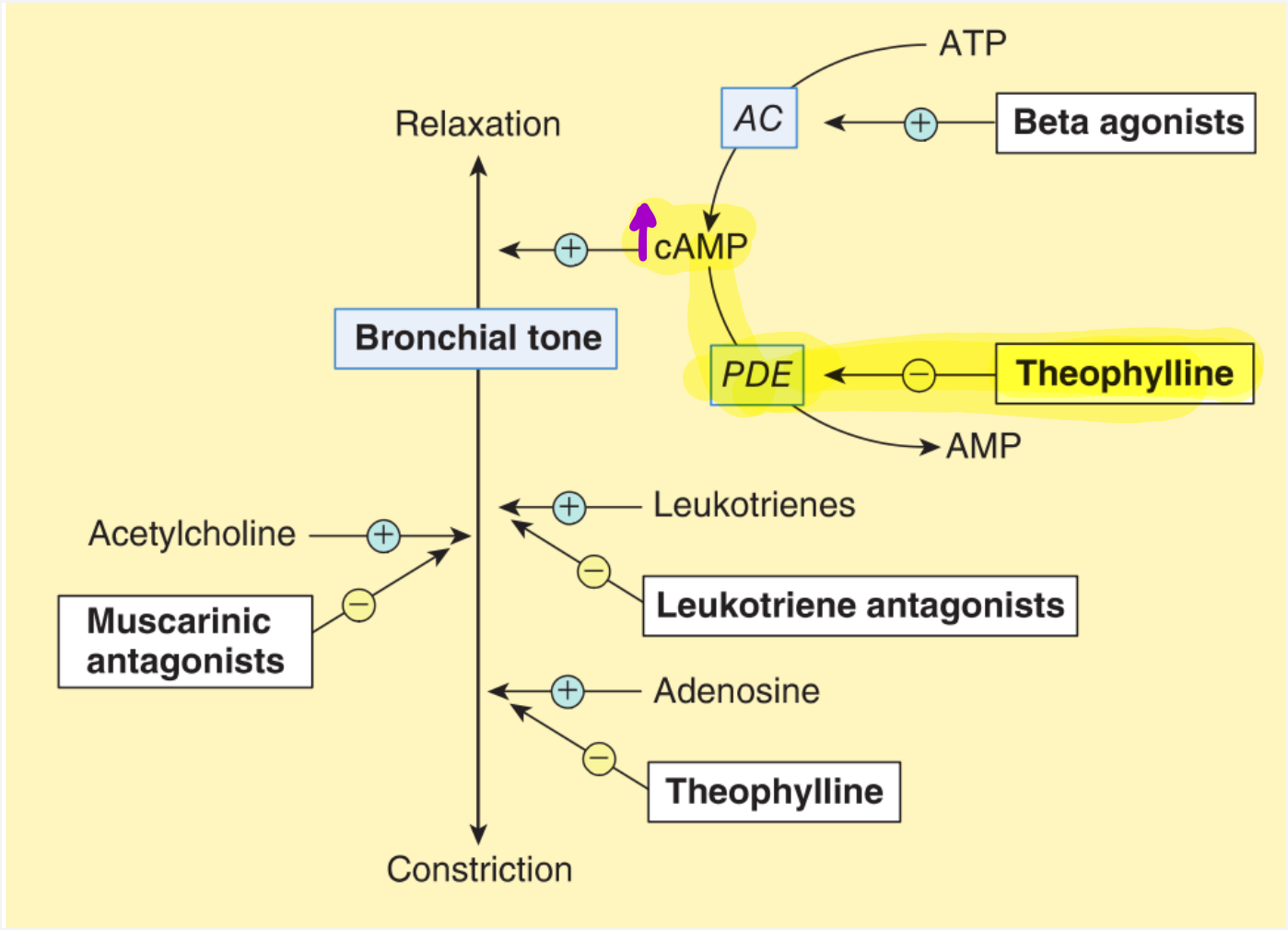


FIGURE 20–5 Structures of theophylline and other methylxanthines.

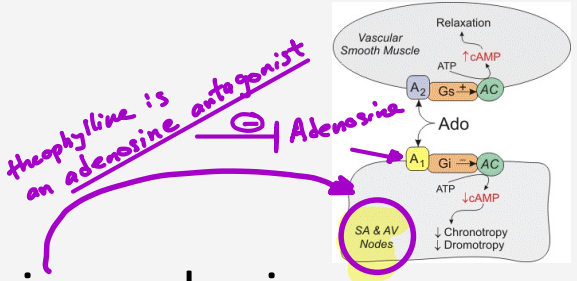

ATP
AC
Beta agonists
Relaxation
cAMP
Bronchial tone
PDE
Theophylline
AMP
Leukotrienes
Acetylcholine
Leukotriene antagonists
Muscarinic antagonists
Adenosine
Theophylline
Constriction

Methylxanthines

Theophylline[A,C]

Mechanism of Action

- Bronchodilation: ⊖ PDE-3 & PDE-4 → ↑ cAMP → ⊕ epi & norepi release → bronchodilation
- Anti-inflammatory effects (mechanism unknown)
- Adenosine receptor antagonist
  - → ↑ Ca^{2+} influx (cardiac cells) → cardiac arrhythmias and seizures
  - → ↓ Ca^{2+} influx (inflammatory cells) → ⊖ intracellular Ca^{2+} release
- Narrow therapeutic index → therapeutic range (10-20 mcg/mL)



Methylxanthines

Theophylline[A,C]

Indication

- Moderate and severe asthma control (rare)
- COPD (rarely used due to side effects)

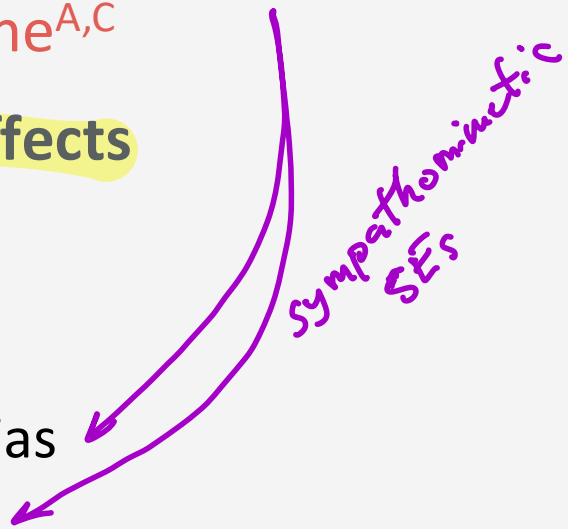
theophylline
3rd - 4th line agent in asthma/COPD

Methylxanthines

Theophylline[A,C]

Adverse Effects

- Nausea
- Vomiting
- Arrhythmias
- Seizures
- Hallucinations, psychosis



Contraindications

- Active peptic ulcer disease
- Seizure disorders

Inhaled Glucocorticoids (ICS)

Inhaled Corticosteroids

Fluticasone[A], Budesonide[A], Beclomethasone[A], Mometasone[A], Ciclesonide[A]

Formulations

- Powder inhalers
- Metered-dose inhalers

ICS
INHALED CORTICOSTEROID

Alvesco 12+
METERED DOSE
(60 inhalations)
Ciclesonide

Arnuity Ellipta 5+
DRY POWDER
(30 inhalations)
Fluticasone furoate

Asmanex Twisthaler 4+
DRY POWDER
(**110 mcg:** 30 inhalations); (**220 mcg:** 120 inhalations)
Mometasone

Asmanex HFA 5+
METERED DOSE
(120 inhalations)
Mometasone

Flovent Diskus *(Brand Discontinued)* 4+ AG
DRY POWDER
(60 inhalations)
Fluticasone propionate

Flovent HFA *(Brand Discontinued)* 4+ AG
METERED DOSE
(120 inhalations)
Fluticasone propionate

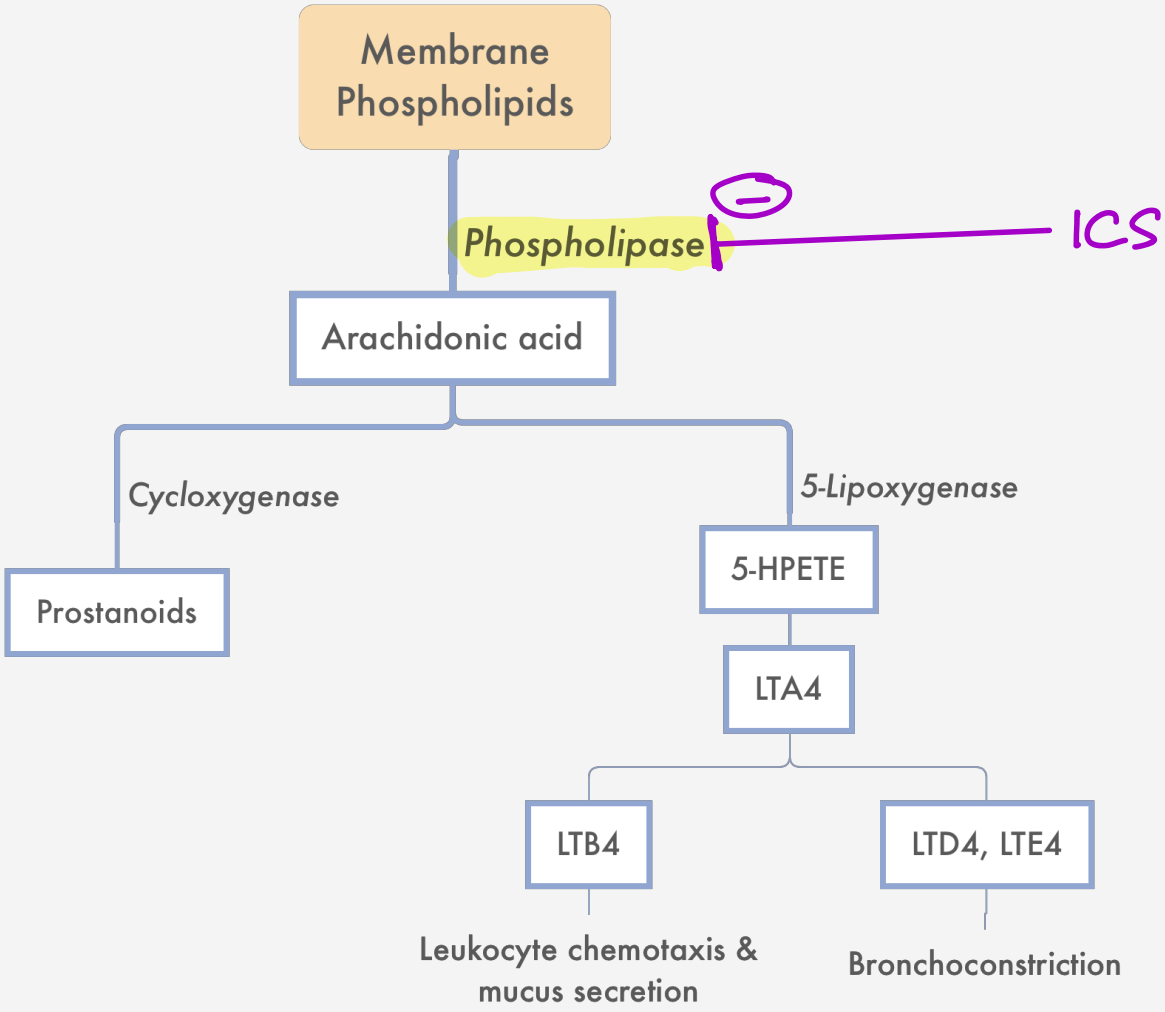
Pulmicort Flexhaler 6+
DRY POWDER
(**90 mcg:** 60 inhalations); (**180 mcg:** 120 inhalations)
Budesonide

QVAR RediHaler 4+
METERED DOSE
(120 inhalations)
Beclomethasone

Age (years) approved for asthma
Age (years) approved for bronchospasm
C Approved for COPD

AG **Authorized generic available**
G **AB-rated generics available**
(including branded generics)

Note: SABAs are FDA-approved for bronchospasm in reversible obstructive airway diseases **and** exercise-induced bronchospasm (EIB), except **Xopenex (levalbuterol)**, which is not indicated for EIB; **Airsupra (albuterol/budesonide)** is indicated as needed for bronchoconstriction and to reduce the risk of asthma exacerbations; **Serevent Diskus (salmeterol)** is indicated for EIB, asthma (**in addition to an ICS**), and COPD. Indications and evidence are subject to change and geographic variability.


Membrane Phospholipids
Phospholipase
ICS
Arachidonic acid
Cycloxygenase
5-Lipoxygenase
Prostanoids
5-HPETE
LTA4
LTB4
LTD4, LTE4
Leukocyte chemotaxis & mucus secretion
Bronchoconstriction

Inhaled Corticosteroids

Fluticasone[A], Budesonide[A], Beclomethasone[A], Mometasone[A], Ciclesonide[A]

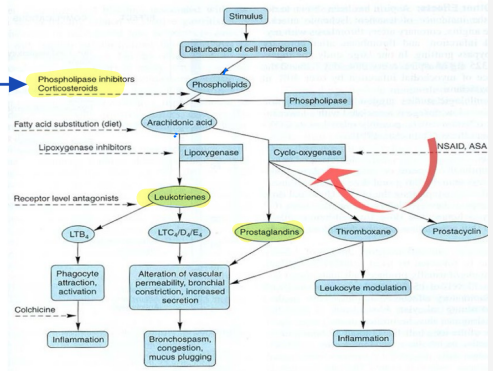
Mechanism of Action

- Inhibit phospholipase A2 → blocks release of arachidonic acid → Inhibit cytokine production (prostaglandins, leukotrienes, thromboxanes) → Reduce airway hyperresponsiveness

Inhaled Corticosteroids (ICS)

Beclomethasone (QVAR), Budesonide (Pulmocort), Fluticasone (Flovent), Triamcinolone (Azmacort), Mometasone (Asmanex), and Flunisolide (AeroBID)

- Mechanisms of Action: ICS are nonspecific suppressors of inflammation
  - ICS inhibit arachidonic acid metabolism, resulting in the decreased production of leukotrienes and prostaglandins
  - ICS reduce the migration and activation of inflammatory cells by inhibiting cytokine production
  - ICS increase the responsiveness of the beta$_2$-receptors of airway smooth muscle



Inhaled Corticosteroids

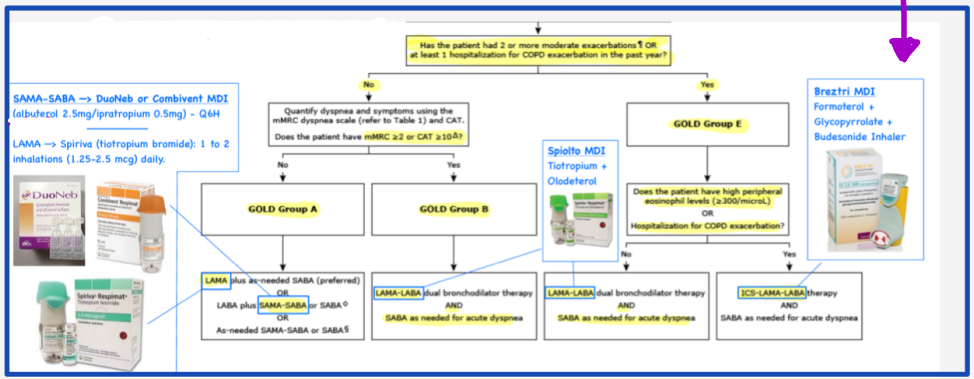
Fluticasone[A], Budesonide[A], Beclomethasone[A], Mometasone[A], Ciclesonide[A]

Indication

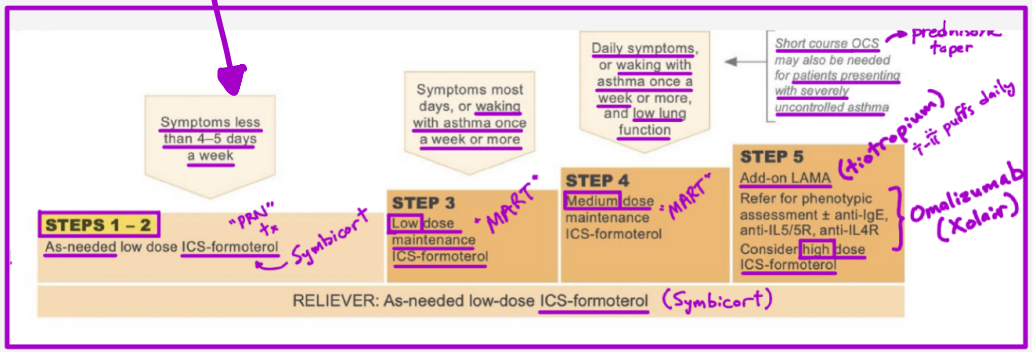
- Asthma control
- COPD control

GOLD Grp E
- eosinophil level > 300
- COPD exacerbation

COPD



Asthma



Inhaled Corticosteroids

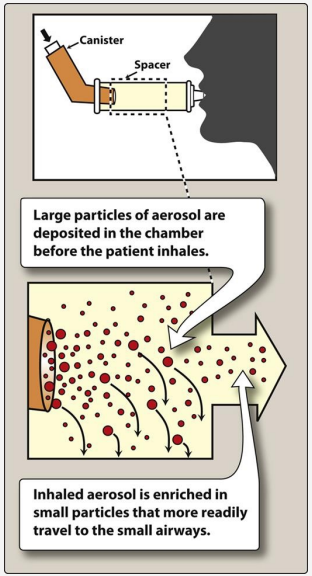
Fluticasone[A], Budesonide[A], Beclomethasone[A], Mometasone[A], Ciclesonide[A]

Adverse Effects

- Oral thrush(*Candida albicans*)
- Hoarseness, cough
- Adrenal suppression (high doses)

Contraindications

- Acute asthma attack, or status asthmaticus (not for rescue therapy)

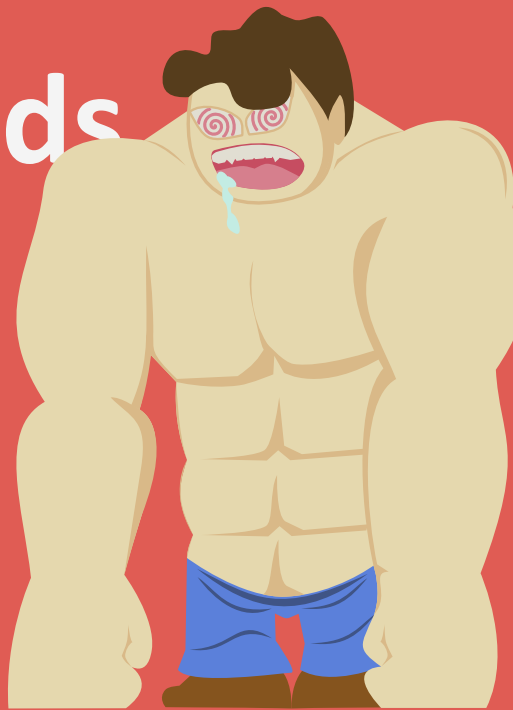


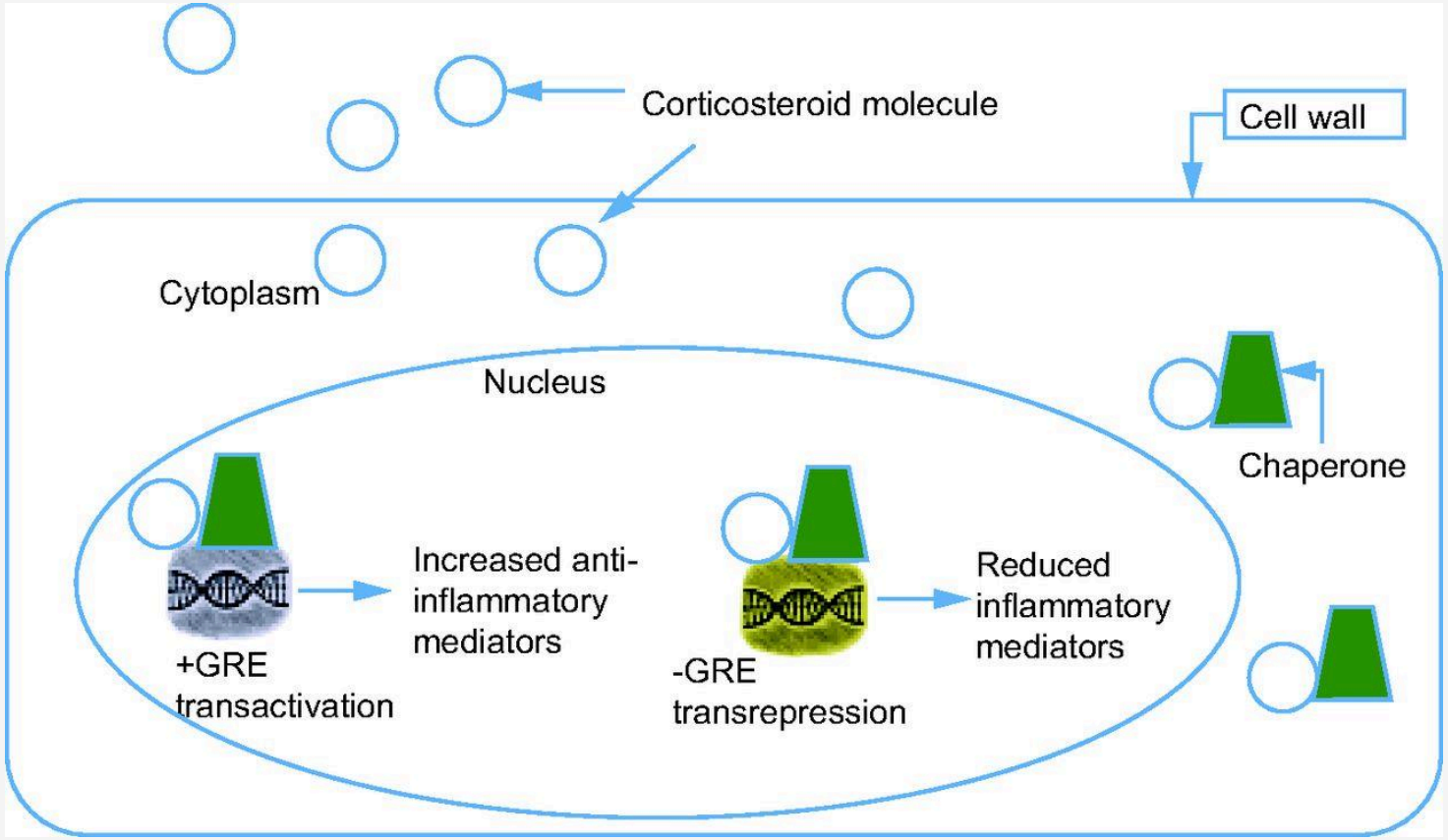
Inhaled Corticosteroids (ICS)

- Side Effects: cough, dysphonia, oral thrush (candidiasis)
  - cough, due to the additive oleic acid, may occur with the use of some corticosteroid inhaler products; but is minimized by the use of spacers
  - reversible dysphonia may occur with deposition of the steroid on vocal cords
  - localized infection with *Candida albicans* may occur in the mouth, pharynx, or the larynx
- Major Adverse Effects of Systemic Corticosteroids

Metabolic & Endocrine Hyperglycemia Adrenal Insufficiency (i.e., HPA-Axis Suppression) Immune System Immunosuppression (risk of infection) Hematologic Leukocytosis Cardiovascular Fluid Retention Hypertension	Neuropsychiatric Dysphoria/Depression Mania/Psychosis Euphoria Insomnia Ophthalmologic Elevated Intraocular Pressure Cataract Formation Exophthalmos Gastrointestinal Gastritis Peptic Ulcer Disease (PUD)	Bone & Muscle Osteoporosis Myopathy Dermatologic & Appearance Cushingoid Appearance Facial Erythema Skin thinning Weight Gain Hirsutism Acne Striae

Systemic Corticosteroids




Corticosteroid molecule
Cell wall
Cytoplasm
Nucleus
Chaperone
Increased anti-inflammatory mediators
+GRE transactivation
-GRE transrepression
Reduced inflammatory mediators

Systemic Corticosteroids

Prednisone, Methylprednisolone, Dexamethasone

Mechanism of Action

- Diffuse across cell membrane → bind GC receptors → binds elements of DNA → upregulation of anti-inflammatory protein expression & downregulation of proinflammatory protein expression → Suppress immune response → Reduce airway inflammation

Systemic:
Methylprednisolone
Prednisolone
Prednisone

Indications

- For short-term (3–10 days) "burst": to gain prompt control of inadequately controlled persistent asthma.
- For long-term prevention of symptoms in severe persistent asthma: suppression, control, and reversal of inflammation.

Mechanisms

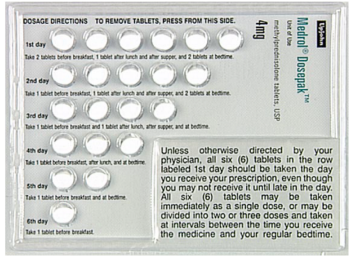
- Same as inhaled.

- Short-term use: reversible abnormalities in glucose metabolism, increased appetite, fluid retention, weight gain, mood alteration, hypertension, peptic ulcer, and rarely aseptic necrosis.
- Long-term use: adrenal axis suppression, growth suppression, dermal thinning, hypertension, diabetes, Cushing's syndrome, cataracts, muscle weakness, and—in rare instances—impaired immune function.
- Consideration should be given to coexisting conditions that could be worsened by systemic corticosteroids, such as herpes virus infections, varicella, tuberculosis, hypertension, peptic ulcer, diabetes mellitus, osteoporosis, and *Strongyloides*.

- Use at lowest effective dose. For long-term use, alternate-day a.m. dosing produces the least toxicity. If daily doses are required, one study shows improved efficacy with no increase in adrenal suppression when administered at 3 p.m. rather than in the morning (Beam et al. 1992).

Oral Corticosteroid Therapy

- Oral corticosteroid therapy can be divided into 2 approaches: (1) "burst" tx and (2) long-term tx
  - Burst Regimens of 7-14 days are appropriate for acute exacerbations of asthma
    - HPA-axis Suppression: Little or no residual effect on the HPA-axis occurs after burst therapy and tapering is not necessary to prevent adrenal insufficiency; however, it is often useful to taper the corticosteroid dose to evaluate the effect of withdrawal on a patient's asthma symptoms
    - Example of Burst Regimen: Prednisone each morning: 60 mg on days 1-3; 50 mg on day4; 40 mg on day 5: 30 mg on day 6; 20 mg on day 7; 10 mg on day 8; 5 mg on day 9-10; then stop. Dispose: Prednisone 10 mg # 35 tablets
    - Medrol Dosepak (methylprednisolone 4 mg tabs) is a convenient and easy-to-use oral corticosteroid taper
  - Side Effects of Long-Term Tx of Systemic Corticosteroids: HPA-axis suppression, weight gain, hypertension, hyperglycemia, osteoporosis, myopathy, psychiatric disturbance, and cataracts

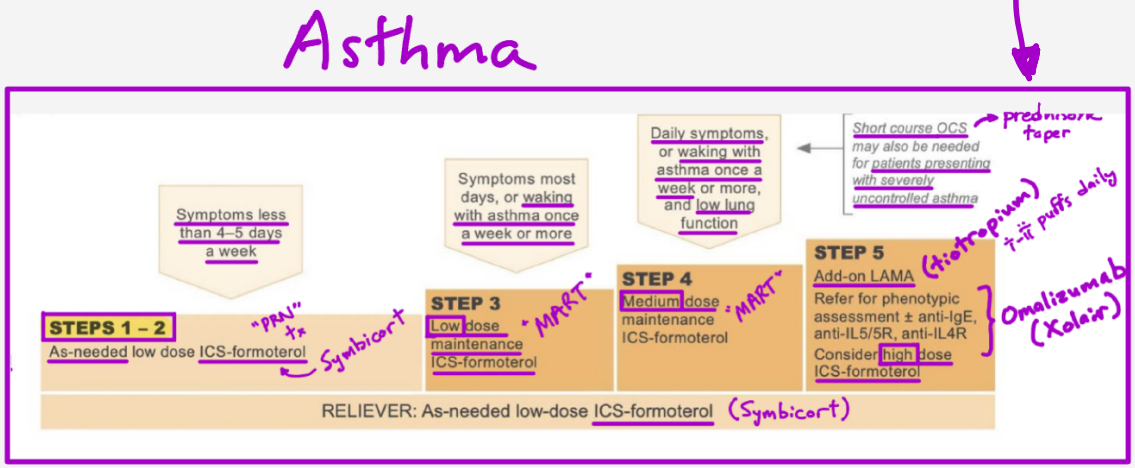


Systemic Corticosteroids

Prednisone, Methylprednisolone, Dexamethasone

Indication

- Severe asthma exacerbations
- COPD exacerbations
- Rheumatologic conditions (eg, RA, severe OA)
- IBD
- Eczema
- Multiple sclerosis
- Adrenal insufficiency
- Many more



Systemic Corticosteroids

Prednisone, Methylprednisolone, Dexamethasone

Adverse Effects

- Hyperglycemia
- Weight gain
- Osteoporosis
- Hypertension
- Behavior change (euphoria
- Adrenal suppression
- Impaired wound healing

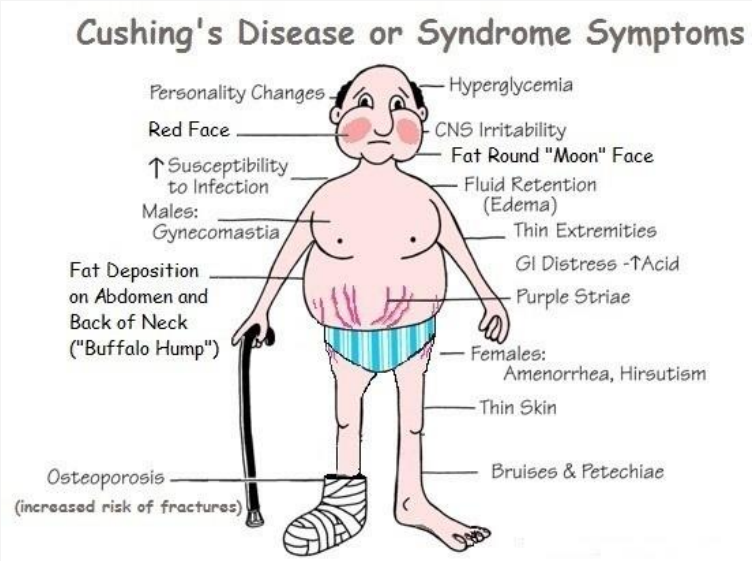
Major Adverse Effects of Systemic Corticosteroids

Metabolic & Endocrine	Neuropsychiatric	Bone & Muscle
Hyperglycemia Adrenal Insufficiency (i.e., HPA-Axis Suppression)	Dysphoria/Depression Mania/Psychosis Euphoria Insomnia	Osteoporosis Myopathy
Immune System	**Ophthalmologic**	**Dermatologic & Appearance**
Immunosuppression (risk of infection)	Elevated Intraocular Pressure Cataract Formation Exophthalmos	Cushingoid Appearance Facial Erythema Skin thinning Weight Gain Hirsutism Acne Striae
Hematologic	**Gastrointestinal**	
Leukocytosis	Gastritis Peptic Ulcer Disease (PUD)	
Cardiovascular		
Fluid Retention Hypertension		

- Short-term use: reversible abnormalities in glucose metabolism, increased appetite, fluid retention, weight gain, mood alteration, hypertension, peptic ulcer, and rarely aseptic necrosis.
- Long-term use: adrenal axis suppression, growth suppression, dermal thinning, hypertension, diabetes, Cushing's syndrome, cataracts, muscle weakness, and—in rare instances—impaired immune function.
- Consideration should be given to coexisting conditions that could be worsened by systemic corticosteroids, such as herpes virus infections, varicella, tuberculosis, hypertension, peptic ulcer, diabetes mellitus, osteoporosis, and *Strongyloides*.

Contraindications

- Systemic fungal infections
- Live vaccines



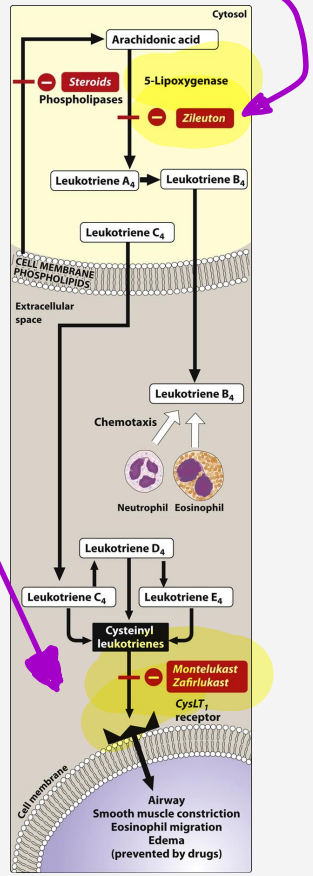
Leukotriene Modifiers

Leukotriene Modifiers

Montelukast[A], Zafirlukast[A], Zileuton[A]

Formulations

- Tablets
- Once daily – Montelukast
- Twice daily – Zafirlukast
- 2-4 times a day – Zileuton



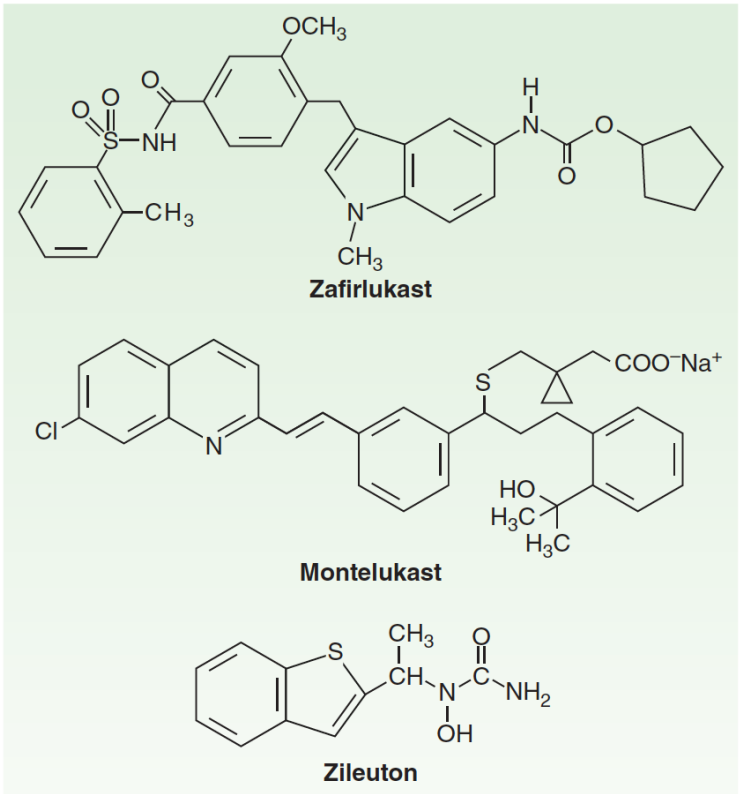


FIGURE 20–7 Structures of leukotriene receptor antagonists (montelukast, zafirlukast) and of the 5-lipoxygenase inhibitor (zileuton).

FIGURE 3–22. LONG-TERM CONTROL MEDICATIONS (CONTINUED)

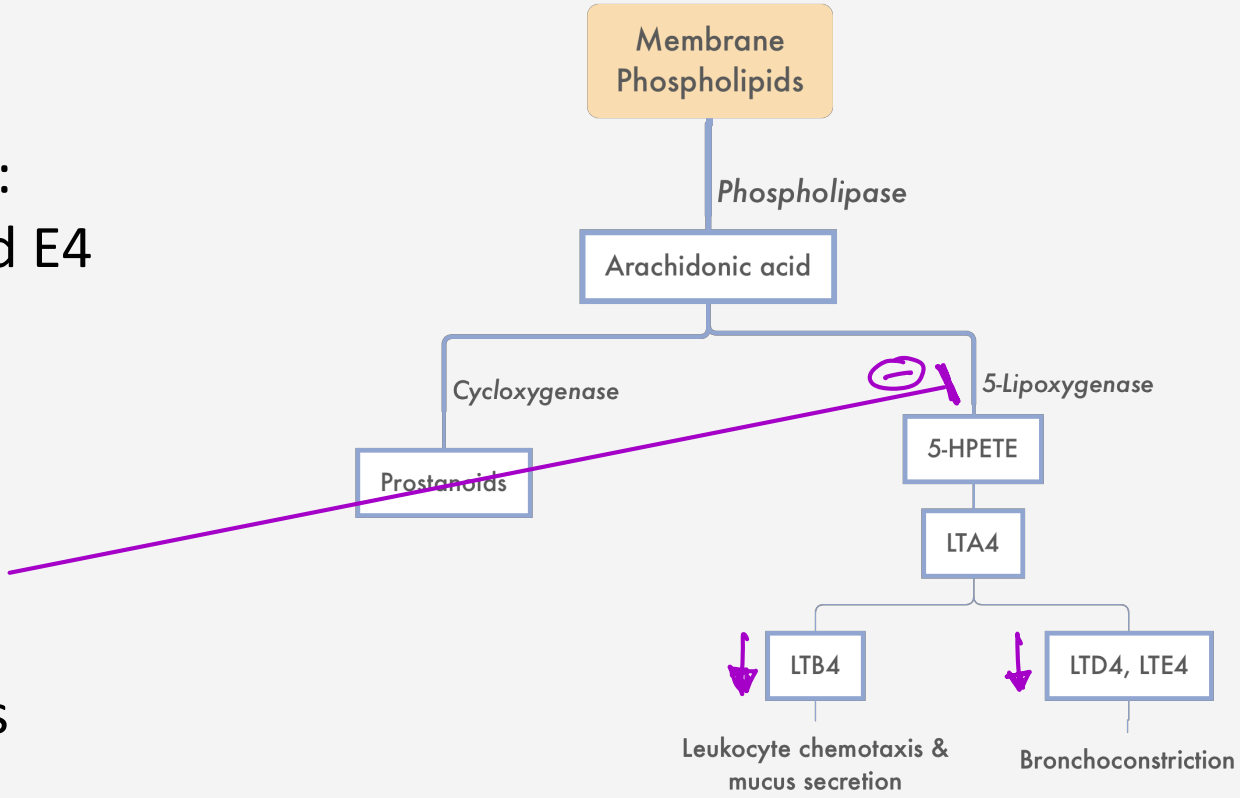
Name/Products (Listed Alphabetically)	Indications/Mechanisms	Potential Adverse Effects	Therapeutic Issues (Not All Inclusive)
Leukotriene Receptor Antagonists (LTRAs)	*Mechanisms* ■ **Leukotriene receptor antagonist;** selective competitive inhibitor of $CysLT_1$ receptor.	neuropsychiatric SEs include sleep disturbances, agitation, depression, suicidal ideation, anxiety. SEs are reversible	■ May attenuate EIB in some patients, but less effective than ICS therapy (Vidal et al. 2001). ■ Do not use LTRA + LABA as a substitute for ICS + LABA.
Montelukast tablets and granules	*Indications* ■ Long-term control and prevention of symptoms in mild persistent asthma for patients ≥1 year of age. May also be used with ICS as combination therapy in moderate persistent asthma.	■ No specific adverse effects have been identified. ■ Rare cases of Churg-Strauss have occurred, but the association is unclear.	■ A flat dose-response curve, without further benefit, if dose is increased above those recommended.
Zafirlukast tablets	■ Long-term control and prevention of symptoms in mild persistent asthma for patients ≥7 years of age. May also be used with ICS as combination therapy in moderate persistent asthma.	■ Postmarketing surveillance has reported cases of reversible hepatitis and, rarely, irreversible hepatic failure resulting in death and liver transplantation.	■ Administration with meals decreases bioavailability; take at least 1 hour before or 2 hours after meals. ■ Zafirlukast is a microsomal P450 enzyme inhibitor that can inhibit the metabolism of warfarin. INRs should be monitored during coadministration. ■ Patients should be warned to discontinue use if they experience signs and symptoms of liver dysfunction (right upper quadrant pain, pruritis, lethargy, jaundice, nausea), and patients' ALTs should be monitored.
5-Lipoxygenase Inhibitor	*Mechanisms* ■ Inhibits the production of leukotrienes from arachidonic acid, both LTB_4 and the cysteinyl leukotrienes.		
Zileuton tablets	*Indications* ■ Long-term control and prevention of symptoms in mild persistent asthma for patients ≥12 years of age. ■ May be used with ICS as combination therapy in moderate persistent asthma in patients ≥12 years of age.	■ Elevation of liver enzymes has been reported. Limited case reports of reversible hepatitis and hyperbilirubinemia.	■ Zileuton is microsomal P450 enzyme inhibitor that can inhibit the metabolism of warfarin and theophylline. Doses of these drugs should be monitored accordingly. ■ Monitor hepatic enzymes (ALT).

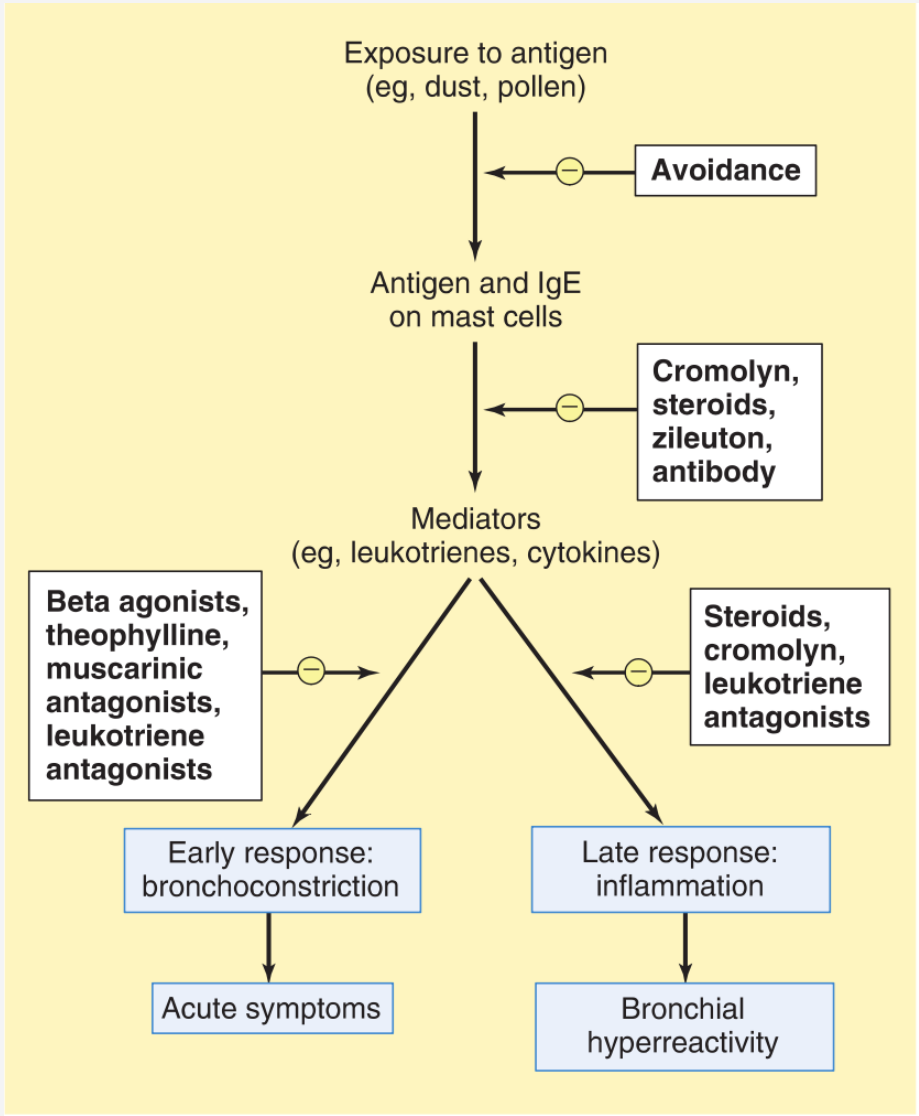
Leukotriene Modifiers

Montelukast[A], Zafirlukast[A], Zileuton[A]

Mechanism of Action

- Montelukast, Zafirlukast: Block leukotriene D4 and E4 receptors → Inhibits bronchoconstriction & inflammation
- Zileuton: Inhibitor of 5-lipoxygenase → reduces synthesis of leukotrienes
- Duration: 12-24 hours




Exposure to antigen
(eg, dust, pollen)
Avoidance
Antigen and IgE
on mast cells
Cromolyn,
steroids,
zileuton,
antibody
Mediators
(eg, leukotrienes, cytokines)
Beta agonists,
theophylline,
muscarinic
antagonists,
leukotriene
antagonists
Steroids,
cromolyn,
leukotriene
antagonists
Early response:
bronchoconstriction
Late response:
inflammation
Acute symptoms
Bronchial
hyperreactivity

Leukotriene Modifiers

Montelukast[A], Zafirlukast[A], Zileuton[A]

Indication

- Asthma control
- Exercise-induced bronchoconstriction
- Allergic rhinitis

added to ICS in moderate persistant asthma

Global Initiative for Asthma (GINA)[3]

Asthma symptoms	Therapy
Step 1	
▪ Infrequent asthma symptoms (eg, <2 times/week) ▪ No risk factors for exacerbations[¶]	▪ Low-dose ICS-formoterol as needed (preferred)[Δ] → Track 1 **or** ▪ Low-dose ICS whenever SABA used or as-needed low-dose ICS-SABA[Δ] → Track 2
Step 2	
▪ Asthma symptoms or need for reliever inhaler ≥2 times/week, but without troublesome daily symptoms	▪ Low-dose ICS-formoterol as needed (preferred) → Track 1 **or** ▪ Low-dose ICS daily **and** SABA as needed → Track 2 **Other options** ▪ Low-dose ICS-SABA or ICS **plus** SABA, concomitantly administered, as needed **or** (less preferred) ▪ LTRA daily **and** SABA as needed
Step 3	
▪ Troublesome asthma symptoms most days, nocturnal awakening due to asthma ≥1 time/month, multiple risk factors for exacerbations[¶]	▪ Low-dose ICS-formoterol as maintenance and reliever therapy[◇] (preferred) → Track 1 **or** ▪ Low-dose ICS-LABA combination daily **and** SABA as needed → Track 2 (Advair or Symbicort) **Other options** ▪ Medium-dose ICS daily **and** SABA or ICS-SABA[Δ] as needed **or** ▪ Low-dose ICS plus LTRA daily **and** SABA or ICS-SABA[Δ] as needed
Step 4	
Severely uncontrolled asthma with ≥3 of the following: ▪ Daytime asthma symptoms >2 times/week ▪ Nocturnal awakening due to asthma ▪ Reliever needed for symptoms >2 times/week ▪ Activity limitation due to asthma	▪ Medium-dose ICS-formoterol as maintenance and reliever therapy[◇] (preferred) **or** ▪ Medium dose ICS-LABA daily **and** SABA or ICS-SABA[Δ] as needed **Other options** ▪ Possible add-on LAMA or switch to ICS-LAMA-LABA ▪ Possible add-on LTRA

Leukotriene Modifiers

Montelukast[A], Zafirlukast[A], Zileuton[A]

impt. Monitor liver enzymes

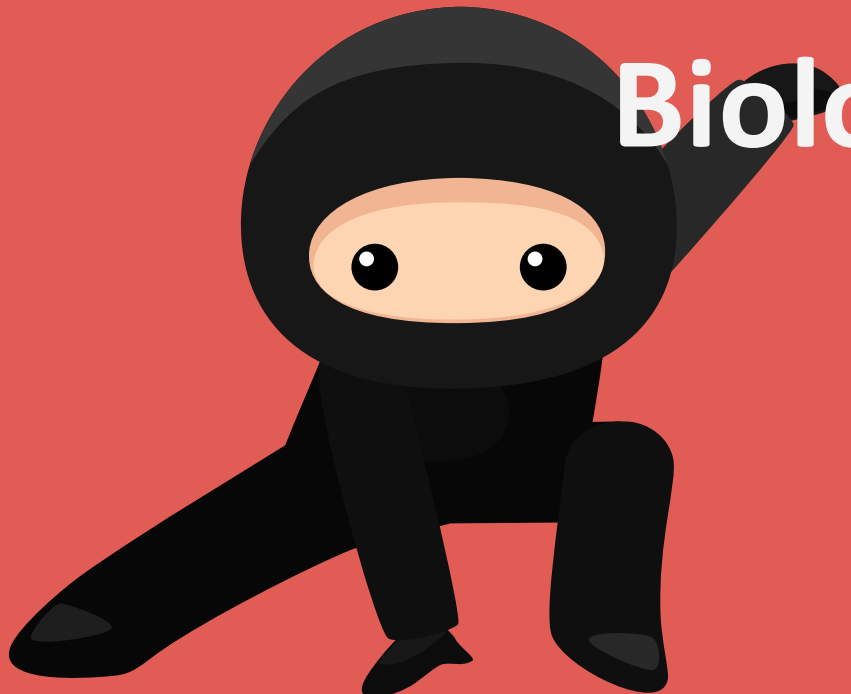
Adverse Effects

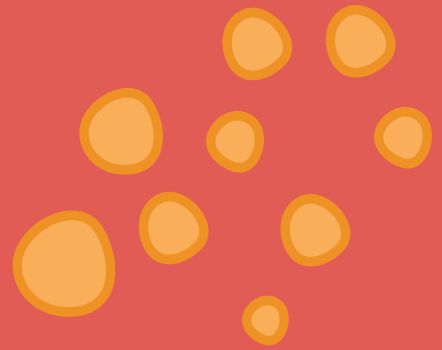
- Abdominal pain (Montelukast)
- Neuropsychiatric events – rare
  - Aggression, hallucinations, irritability, SI
- Headache (Zafirlukast)
- Eosinophilic granulomatosis with polyangiitis (EGPA)

Contraindications

- Hypersensitivity
- Hepatic impairment

Biologic Agents





Monoclonal Antibodies

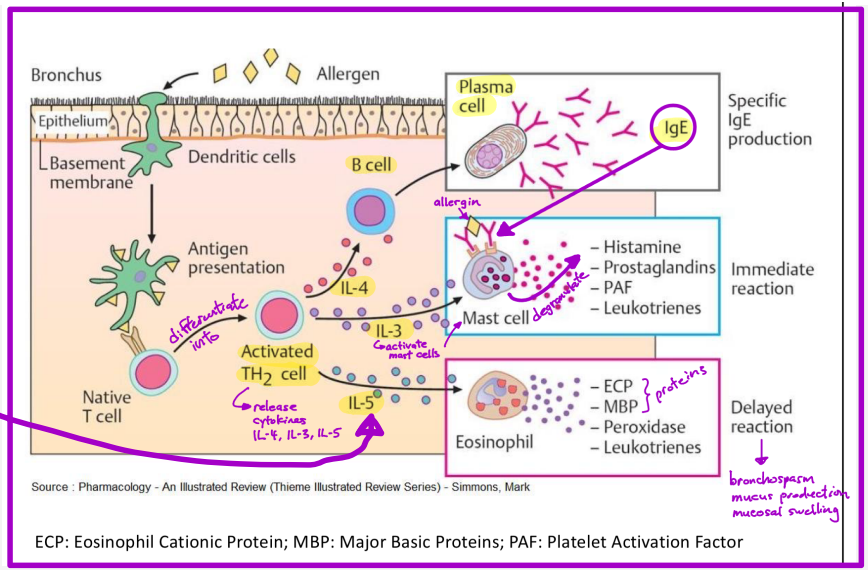
Omalizumab, Mepolizumab, Benralizumab

target IGE

target IL-5 in eosinophilic asthma

Formulations

- Subcutaneous injections, every 2-4 weeks



ECP: Eosinophil Cationic Protein; MBP: Major Basic Proteins; PAF: Platelet Activation Factor

indication of omalizumab: mod-severe persistent allergic asthma not controlled by ICS

Xolair prices

Subcutaneous Powder For Injection

150 mg
Xolair subcutaneous powder for injection

from **$1,487.68**
for 1 powder for injection

Quantity	Per unit	Price
1	$1,487.68	$1,487.68

Important: When there is a range of pricing, consumers should normally expect to pay the lower price. However, due to stock shortages and other unknown variables we cannot provide any guarantee.

Immunomodulators

Omalizumab
(Anti-IgE)

For subcutaneous use

Indications

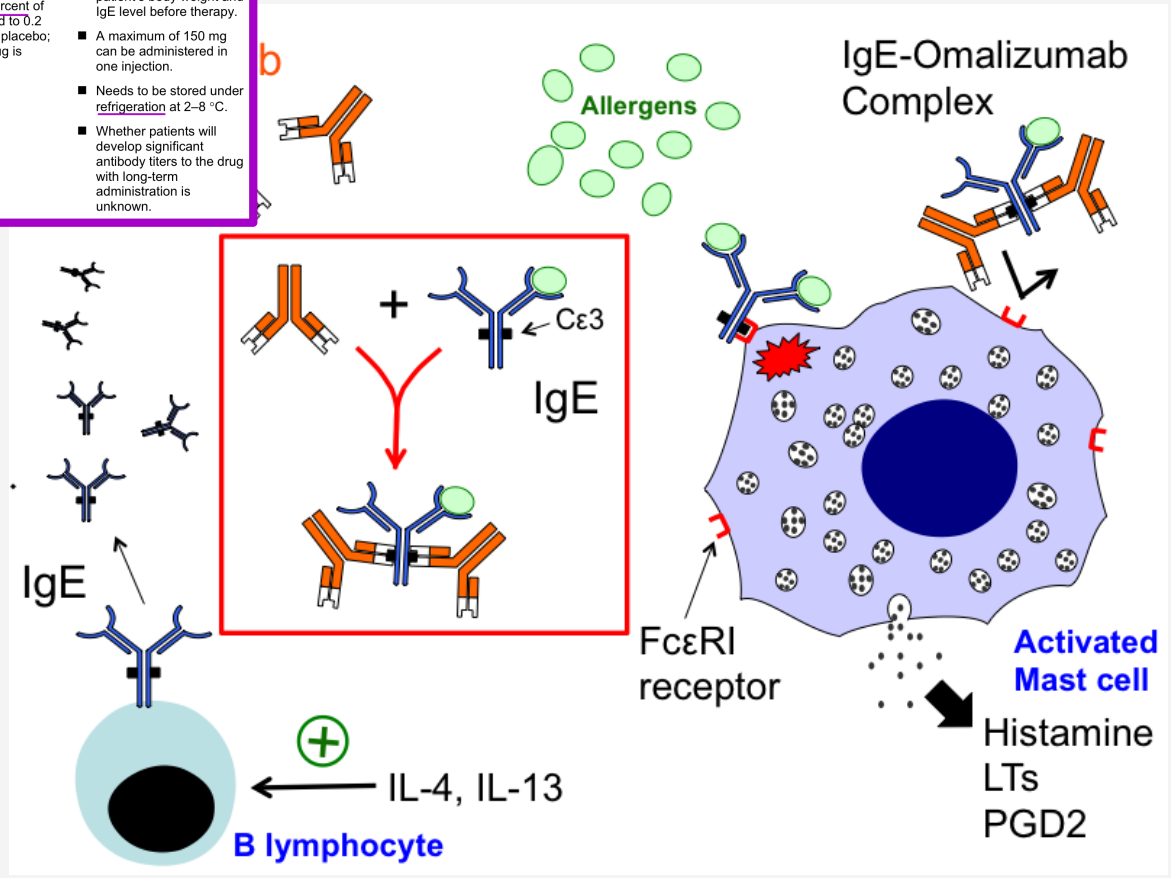
- Long-term control and prevention of symptoms in adults (≥12 years old) who have moderate or severe persistent allergic asthma inadequately controlled with ICS.

Mechanisms

- Binds to circulating IgE, preventing it from binding to the high-affinity (FcεRI) receptors on basophils and mast cells.
- Decreases mast cell mediator release from allergen exposure.
- Decreases the number of FcεRIs in basophils and submucosal cells.

- Pain and bruising of injection sites has been reported in 5–20 percent of patients.
- Anaphylaxis has been reported in 0.2 percent of treated patients.
- Malignant neoplasms were reported in 0.5 percent of patients compared to 0.2 percent receiving placebo; relationship to drug is unclear.

- Monitor patients following injection. Be prepared and equipped to identify and treat anaphylaxis that may occur.
- The dose is administered either every 2 or 4 weeks and is dependent on the patient's body weight and IgE level before therapy.
- A maximum of 150 mg can be administered in one injection.
- Needs to be stored under refrigeration at 2–8 °C.
- Whether patients will develop significant antibody titers to the drug with long-term administration is unknown.

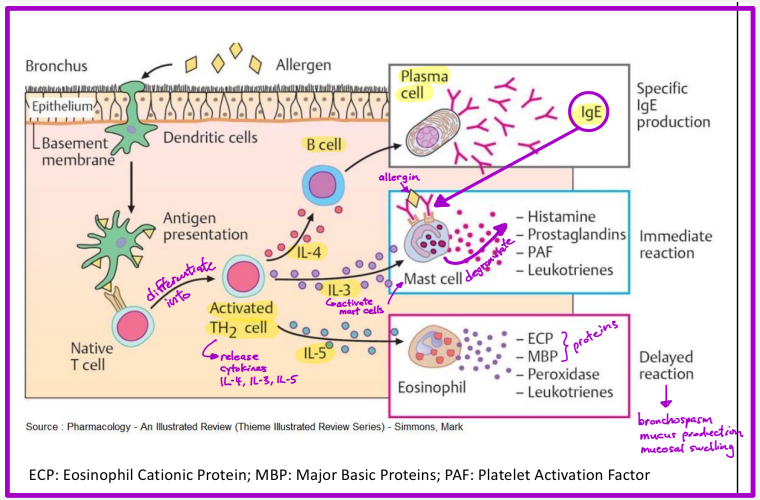


Monoclonal Antibodies

Omalizumab, Mepolizumab, Benralizumab

Mechanism of Action

- Omalizumab: Binds IgE → Prevents binding to receptor on mast cells, basophils → reduce allergen-IgE interaction
- Mepolizumab/Benralizumab: IL-5 antagonists → Reduce eosinophilic inflammation



ECP: Eosinophil Cationic Protein; MBP: Major Basic Proteins; PAF: Platelet Activation Factor

Monoclonal Antibodies

Omalizumab, Mepolizumab, Benralizumab

Indication

- Severe allergic asthma (IgE antibody-mediated)
  - Not controlled by ICS
  - IgE between 30-700 IU/mL
- Chronic spontaneous urticaria
  - Not controlled with H_1 antihistamines

Monoclonal Antibodies

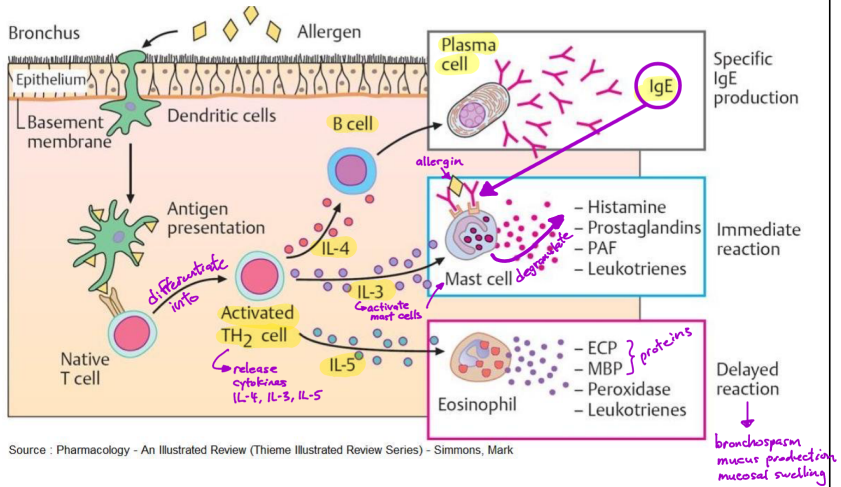
Omalizumab, Mepolizumab, Benralizumab

Adverse Effects

- Injection site reactions
- Anaphylaxis (rare)
- Headache

Contraindications

- Hypersensitivity
- Acute bronchospasm



ECP: Eosinophil Cationic Protein; MBP: Major Basic Proteins; PAF: Platelet Activation Factor

Monoclonal Antibodies

Omalizumab, Mepolizumab, Benralizumab

eosinophilic asthma

TABLE 20–1 Monoclonal antibodies for use in asthma.[1]

Antibody Name	Isotype	Target
Omalizumab	Humanized IgG1	IgE
Mepolizumab	Humanized IgG1	IL-5
Benralizumab	Humanized IgG1	IL-5 receptor
Reslizumab	Humanized IgG4	IL-5
Dupilumab	Humanized IgG4	IL-4 receptor

[1]Approved or in phase 2 or 3 clinical trials.

Phosphodiesterase-4 Inhibitor

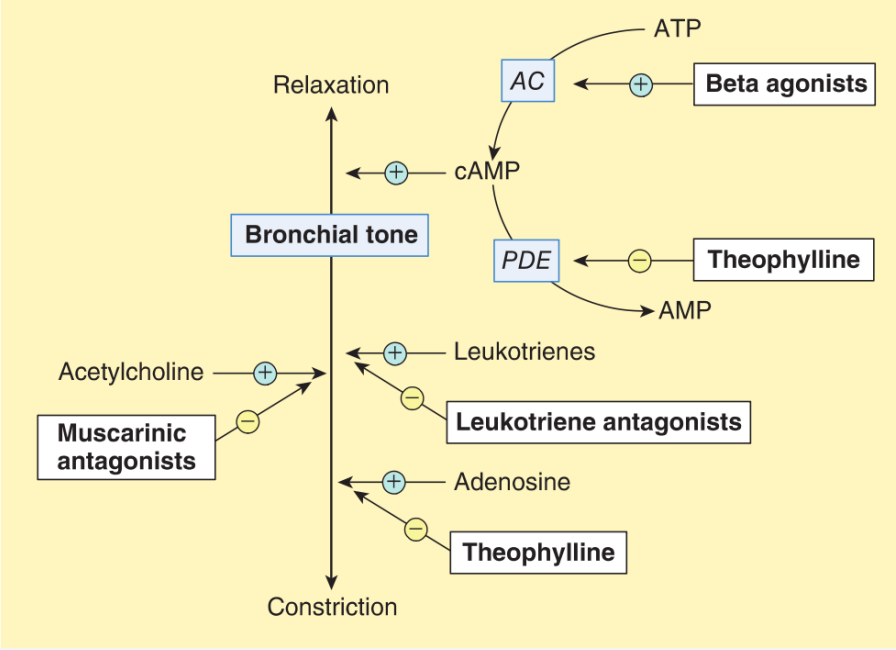
Phosphodiesterase-4 Inhibitors

Roflumilast

Mechanism of Action

↓ cytokine release by neutrophils

- Inhibit PDE-4 → Increase cAMP → Reduce inflammation in airways



Phosphodiesterase-4 Inhibitors

Roflumilast

Indication

- Severe COPD with chronic bronchitis

Phosphodiesterase-4 Inhibitors

Roflumilast

Adverse Effects

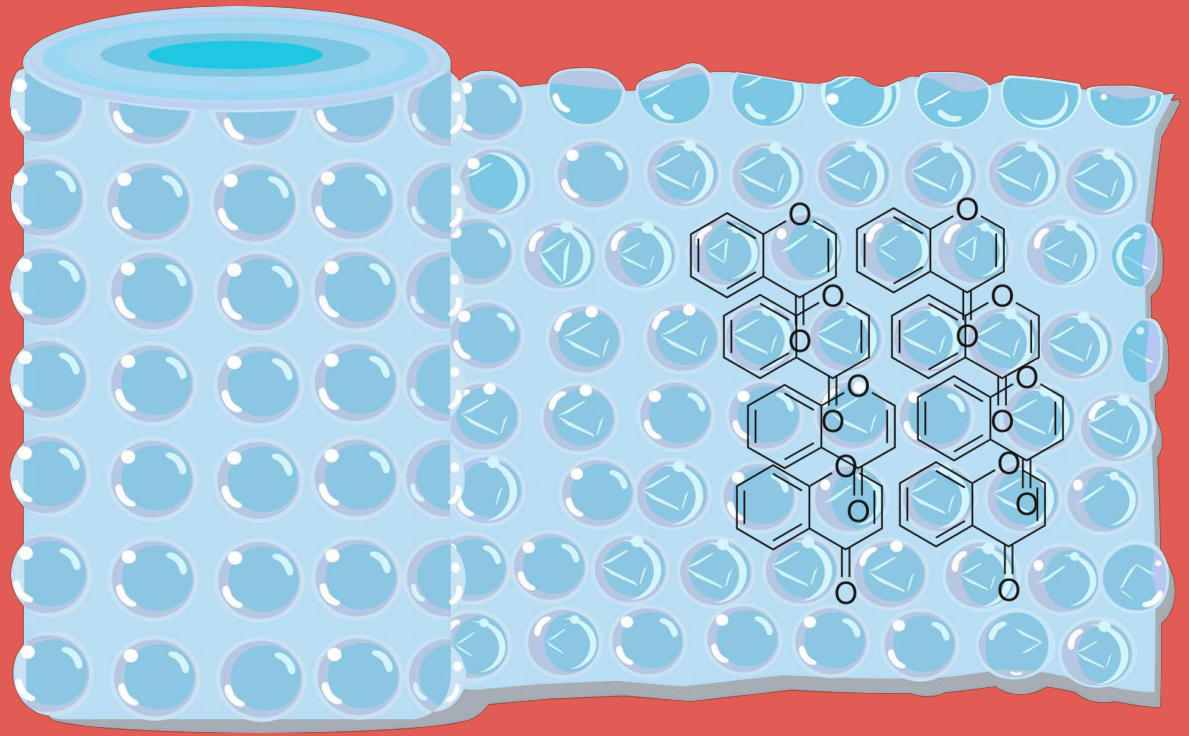
- Diarrhea
- Weight loss
- Depression
- Insomnia

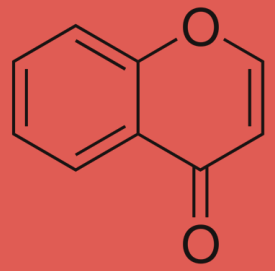
neuropsychiatric SEs

Contraindications

- Moderate to severe liver impairment

Mast Cell Stabilizers





Mast Cell Stabilizers

Cromolyn sodium, Nedocromil

Formulations

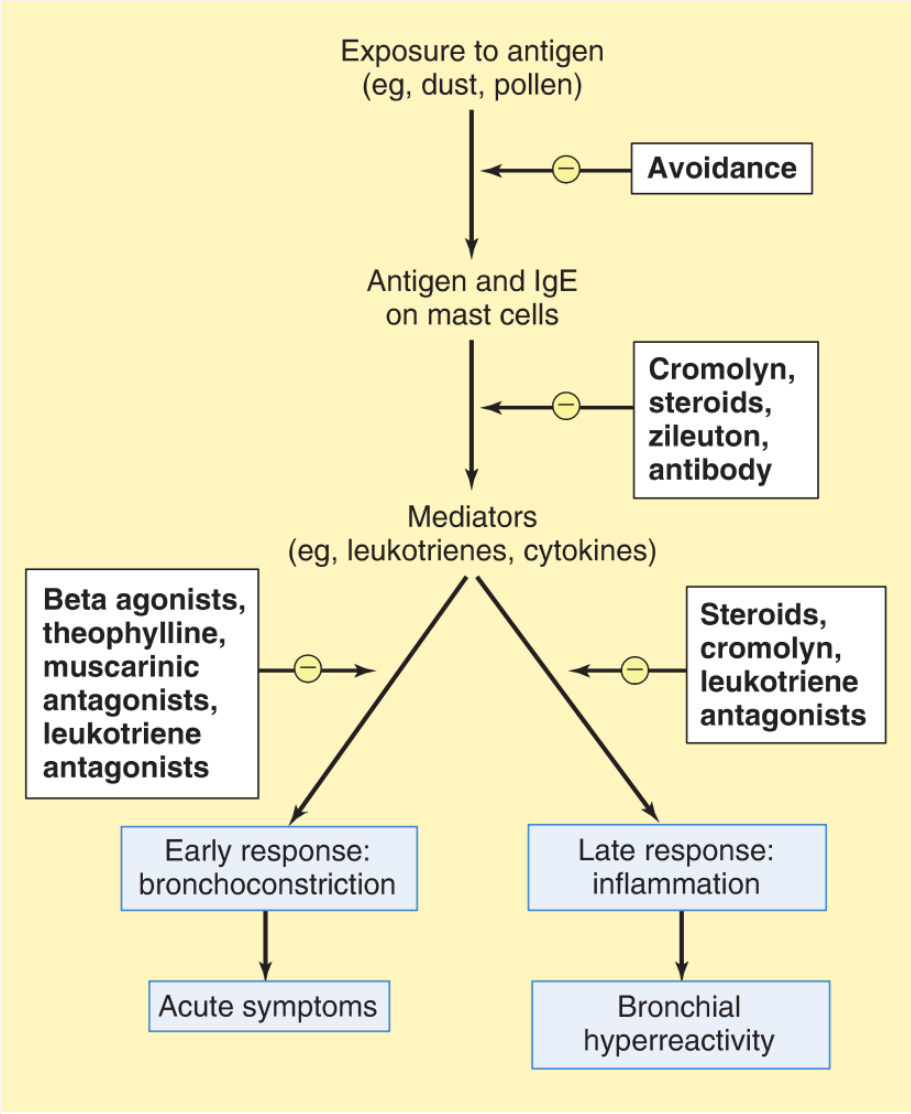
- Inhaled solution, nasal spray, eye drops (other conditions)
- Duration: 3-6h

Mast Cell Stabilizers

Cromolyn sodium, Nedocromil

Mechanism of Action

- Inhibit mast cell degranulation → Prevent release of histamine and inflammatory mediators

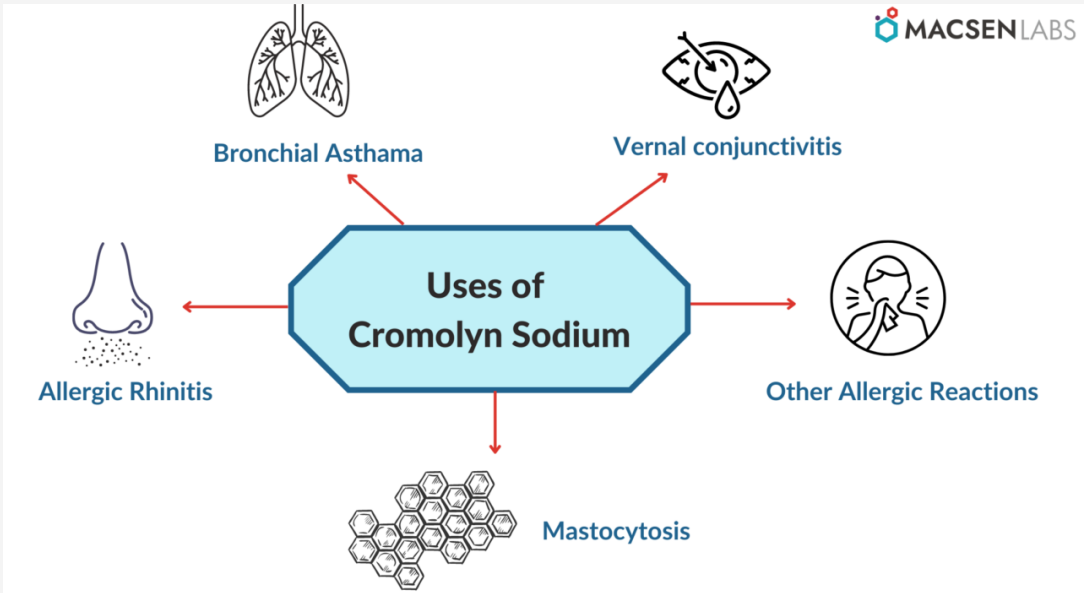


Mast Cell Stabilizers

Cromolyn sodium, Nedocromil

Indication

- Asthma prophylaxis (rarely used)
- Allergic rhinitis



Mast Cell Stabilizers

Cromolyn sodium, Nedocromil

Adverse Effects

- Cough
- Throat irritation
- Unpleasant taste
  with nedocromil

Contraindications

- Hypersensitivity

Cromolyn (Intal) & Nedocromil (Tilade) Inhalers

- Cromolyn and nedocromil are non-steroidal, but less potent anti-inflammatory agents
- Mechanism of Action: Cromolyn and nedocromil stabilize the mast cell membrane
  → prevents degranulation of mast cells
  → inhibits release of inflammatory mediators (i.e., histamine, leukotrienes, prostaglandins)
- Side Effects: Cough and throat irritation
  - Cromolyn and nedocromil are generally well tolerated have favorable side effect profiles and may be considered for use in patients with mild asthma
- Concomitant therapy with cromolyn or nedocromil with inhaled corticosteroids may permit reduction in the dose of ICS in patients requiring high doses of the latter

Recap

Condition		1st Line Medications	Other Medications	Considerations
Asthma	Acute	Albuterol (SABA)	Ipratropium (SAMA), Systemic Corticosteroids	Rescue inhaler; may cause tremors & tachycardia. SAMA used in severe cases.
Asthma	Chronic	ICS (Fluticasone, Budesonide) ± LABA (Salmeterol)	LTRA (Montelukast), Theophylline, LAMA (Tiotropium)	ICS is the mainstay; LABA must always be combined with ICS in asthma. Montelukast: watch for neuropsychiatric side effects.
COPD	Acute	Albuterol (SABA) + Ipratropium (SAMA)	Systemic Corticosteroids	First-line for acute COPD exacerbations; combo is preferred. Avoid prolonged steroid use.
COPD	Chronic	LAMA (Tiotropium) ± LABA (Salmeterol)	ICS (Fluticasone) in severe cases, Roflumilast (PDE-4 Inhibitor)	LAMA preferred for COPD; ICS only in severe cases (risk of pneumonia). Roflumilast used for severe COPD with chronic bronchitis.

*Refer to clinical medicine lecture and Current Medical Dx&Tx

SABA
SHORT-ACTING BETA-2 AGONIST

ProAir HFA 4+
METERED DOSE
(200 inhalations)
G AG
Albuterol

ProAir RespiClick 4+
DRY POWDER
(200 inhalations)
Albuterol

Proventil HFA 4+
METERED DOSE
(200 inhalations)
G AG
Albuterol

Ventolin HFA 4+
METERED DOSE
(200 inhalations)
AG
Albuterol

Xopenex HFA 4+
METERED DOSE
(200 inhalations)
AG
Levalbuterol

SAMA
SHORT-ACTING MUSCARINIC ANTAGONIST

Atrovent HFA C
METERED DOSE
(200 inhalations)
Ipratropium

SAMA + SABA
COMBINATION

Combivent Respimat C
SOFT MIST
(120 inhalations)
Ipratropium/Albuterol

SABA
SHORT-ACTING BETA-2 AGONIST

ProAir HFA 4+
METERED DOSE
(200 inhalations)
G AG
Albuterol

ProAir RespiClick 4+
DRY POWDER
(200 inhalations)
Albuterol

Proventil HFA 4+
METERED DOSE
(200 inhalations)
G AG
Albuterol

Ventolin HFA 4+
METERED DOSE
(200 inhalations)
AG
Albuterol

Xopenex HFA 4+
METERED DOSE
(200 inhalations)
AG
Levalbuterol

SAMA
SHORT-ACTING MUSCARINIC ANTAGONIST

Atrovent HFA C
METERED DOSE
(200 inhalations)
Ipratropium

SAMA + SABA
COMBINATION

Combivent Respimat C
SOFT MIST
(120 inhalations)
Ipratropium/Albuterol

4+ Age (years) approved for asthma
4+ Age (years) approved for bronchospasm
C Approved for COPD
AG Authorized generic available
G AB-rated generics available
(including branded generics)

NOTE: SABAs are FDA-approved for bronchospasm in reversible obstructive airway diseases *and* exercise-induced bronchospasm (EIB), except Xopenex (levalbuterol) is not indicated for EIB; Airsupra (albuterol/budesonide) is indicated as needed for bronchoconstriction and to reduce the risk of asthma exacerbations; Serevent Diskus (salmeterol) is indicated for EIB, asthma (*in addition to an ICS*), and COPD. Indications and evidence for individual agents are subject to change and geographic variability.

LABA
LONG-ACTING BETA-2 AGONIST

Serevent Diskus 4+ 4+ C
DRY POWDER
(60 inhalations)
Salmeterol

Striverdi Respimat C
SOFT MIST
(60 inhalations)
Olodaterol

LAMA
LONG-ACTING MUSCARINIC ANTAGONIST

Incruse Ellipta C
DRY POWDER
(30 inhalations)
Umeclidinium

Spiriva HandiHaler C G
DRY POWDER
(30 doses [2 inhalations/capsule])
Tiotropium

Spiriva Respimat 6+ C
SOFT MIST
(60 inhalations)
Tiotropium

Tudorza Pressair C
DRY POWDER
(60 inhalations)
Aclidinium

LAMA + LABA
COMBINATION

Anoro Ellipta C
DRY POWDER
(30 inhalations)
Umeclidinium/Vilanterol

Bevespi Aerosphere C
METERED DOSE
(120 inhalations)
Glycopyrrolate/Formoterol

Duaklir Pressair C
DRY POWDER
(60 inhalations)
Aclidinium/Formoterol

Stiolto Respimat C
SOFT MIST
(60 inhalations)
Tiotropium/Olodaterol

ICS
INHALED CORTICOSTEROID

Alvesco 12+
METERED DOSE
(60 inhalations)
Ciclesonide

Arnuity Ellipta 5+
DRY POWDER
(30 inhalations)
Fluticasone furoate

Asmanex Twisthaler 4+
DRY POWDER
(**110 mcg:** 30 inhalations); (**220 mcg:** 120 inhalations)
Mometasone

Asmanex HFA 5+
METERED DOSE
(120 inhalations)
Mometasone

Flovent Diskus (Brand Discontinued) 4+
DRY POWDER
(60 inhalations)
AG
Fluticasone propionate

Flovent HFA (Brand Discontinued) 4+
METERED DOSE
(120 inhalations)
AG
Fluticasone propionate

Pulmicort Flexhaler 6+
DRY POWDER
(**90 mcg:** 60 inhalations); (**180 mcg:** 120 inhalations)
Budesonide

QVAR RediHaler 4+
METERED DOSE
(120 inhalations)
Beclomethasone

ICS + LAMA + LABA
COMBINATION

Breztri Aerosphere C
METERED DOSE
(120 inhalations)
Budesonide/
Glycopyrrolate/Formoterol

Trelegy Ellipta 18+ C
DRY POWDER
(30 inhalations)
Fluticasone furoate/
Umeclidinium/Vilanterol

SABA + ICS
COMBINATION

Airsupra 18+
METERED DOSE
(120 inhalations)
Albuterol/Budesonide

ICS + LABA
COMBINATION

Advair Diskus 4+ C
DRY POWDER
(60 inhalations)
G AG
Fluticasone prop./Salmeterol

Advair HFA 12+
METERED DOSE
(120 inhalations)
AG
Fluticasone prop./Salmeterol

AirDuo RespiClick 12+
DRY POWDER
(60 inhalations)
AG
Fluticasone prop./Salmeterol

Breo Ellipta 5+ C
DRY POWDER
(30 inhalations)
AG
Fluticasone furoate/Vilanterol

Breyna *(Generic for Symbicort)* 6+ C
METERED DOSE
(120 inhalations)
Budesonide/Formoterol

Dulera 5+
METERED DOSE
(120 inhalations)
Mometasone/Formoterol

Symbicort 6+ C
METERED DOSE
(120 inhalations)
G AG
Budesonide/Formoterol

Wixela Inhub *(Generic for Advair Diskus)* 4+ C
DRY POWDER
(60 inhalations)
Fluticasone prop./Salmeterol

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A = Age (years) approved for asthma
B = Age (years) approved for bronchospasm
C = Approved for COPD

AG = Authorized generic available
G = AB-rated generics available (including branded generics)

Note: SABAs are FDA-approved for bronchospasm in reversible obstructive airway diseases **and** exercise-induced bronchospasm (EIB), except Xopenex (levalbuterol), which is not indicated for EIB. Airsupra (albuterol/budesonide) is indicated as needed for bronchoconstriction and to reduce the risk of asthma exacerbations. Serevent Diskus (salmeterol) is indicated for EIB, asthma **(in addition to an ICS)**, and COPD. Indications and evidence are subject to change and geographic variability.

Aclidinium — TUDORZA PRESSAIR 400 mcg — C
Long-Acting Muscarinic Antagonist

Aclidinium/Formoterol — DUAKLIR PRESSAIR 400/12 mcg — C
Long-Acting Muscarinic Antagonist/
Long-Acting Beta-2 Agonist

Albuterol — PROAIR, PROVENTIL, VENTOLIN 90 mcg — 4+ G AG
Short-Acting Beta-2 Agonist
Note: No generic currently available for ProAir RespiClick

Albuterol/Budesonide — AIRSUPRA 90/80 mcg — 12+
Short-Acting Beta-2 Agonist/
Inhaled Corticosteroid

Beclomethasone — QVAR REDIHALER 40, 80 mcg — 4+
Inhaled Corticosteroid

Budesonide — PULMICORT FLEXHALER 90, 180 mcg — 6+
Inhaled Corticosteroid

Budesonide/Formoterol — SYMBICORT 80/4.5, 160/4.5 mcg — 6+ C G AG
Inhaled Corticosteroid/
Long-Acting Beta-2 Agonist
Breyna is a generic for Symbicort

Budesonide/Glycopyrrolate/Formoterol — BREZTRI AEROSPHERE 160/9/4.8 mcg — C
Inhaled Corticosteroid/
Long-Acting Muscarinic Antagonist/Long-Acting Beta-2 Agonist

Ciclesonide — ALVESCO 80, 160 mcg — 12+
Inhaled Corticosteroid

Fluticasone furoate — ARNUITY ELLIPTA 50, 100, 200 mcg — 5+
Inhaled Corticosteroid

Fluticasone propionate — FLOVENT DISKUS 50, 100, 250 mcg — 4+ AG
Inhaled Corticosteroid
Note: Flovent branded products **discontinued**
FLOVENT HFA 44, 110, 220 mcg — 4+ AG

Fluticasone/Salmeterol — AIRDUO RESPICLICK 55/14, 113/14, 232/14 mcg — 12+ AG
Inhaled Corticosteroid/
Long-Acting Beta-2 Agonist
ADVAIR DISKUS 100/50, 250/50, 500/50 mcg — 4+ C G AG
Wixela Inhub is a generic for Advair Diskus
ADVAIR HFA 45/21, 115/21, 230/21 mcg — 12+ AG

Fluticasone/Umeclidinium/Vilanterol — TRELEGY ELLIPTA 100/62.5/25 mcg, 200/62.5/25 mcg — 18+ C
Inhaled Corticosteroid/
Long-Acting Muscarinic Antagonist/Long-Acting Beta-2 Agonist

Fluticasone/Vilanterol — BREO ELLIPTA 50/25, 100/25, 200/25 mcg — 5+ C AG
Inhaled Corticosteroid/
Long-Acting Beta-2 Agonist

Glycopyrrolate/Formoterol — BEVESPI AEROSPHERE 9/4.8 mcg — C
Long-Acting Muscarinic Antagonist/
Long-Acting Beta-2 Agonist

Ipratropium — ATROVENT HFA 17 mcg — C
Short-Acting Muscarinic Antagonist

Ipratropium/Albuterol — COMBIVENT RESPIMAT 20/100 mcg — C
Short-Acting Muscarinic Antagonist/
Short-Acting Beta-2 Agonist

Levalbuterol — XOPENEX 45 mcg — 4+ AG
Short-Acting Beta-2 Agonist

Mometasone — ASMANEX TWISTHALER 110, 220 mcg — 4+
Inhaled Corticosteroid
ASMANEX HFA 50, 100, 200 mcg — 5+

Mometasone/Formoterol — DULERA 50/5, 100/5, 200/5 mcg — 5+
Inhaled Corticosteroid/
Long-Acting Beta-2 Agonist

Olodaterol — STRIVERDI RESPIMAT 2.5 mcg — C
Long-Acting Beta-2 Agonist

Salmeterol — SEREVENT DISKUS 50 mcg — 4+ 4A C
Long-Acting Beta-2 Agonist

Tiotropium — SPIRIVA HANDIHALER 18 mcg — C G
Long-Acting Muscarinic Antagonist
SPIRIVA RESPIMAT 1.25, 2.5 mcg — 6+ C

Tiotropium/Olodaterol — STIOLTO RESPIMAT 2.5/2.5 mcg — C
Long-Acting Muscarinic Antagonist/
Long-Acting Beta-2 Agonist

Umeclidinium — INCRUSE ELLIPTA 62.5 mcg — C
Long-Acting Muscarinic Antagonist

Umeclidinium/Vilanterol — ANORO ELLIPTA 62.5/25 mcg — C
Long-Acting Muscarinic Antagonist/
Long-Acting Beta-2 Agonist

ICS DAILY DOSE CATEGORIZATION

IN ADULTS AND CHILDREN AGES 6 YEARS AND UP

ICS (DELIVERY)	TOTAL DAILY DOSE (MCG/DAY) Age	Low	Medium	High
Beclomethasone (MDI)	12+ years	100-200	>200-400	>400
	6-11 years	50-100	>100-200	>200
Budesonide (DPI)	12+ years	200-400	>400-800	>800
	6-11 years	100-200	>200-400	>400
Ciclesonide (MDI)	12+ years	80-160	>160-320	>320
	6-11 years	80	>80-160	>160
Fluticasone furoate (DPI)	12+ years	100	100	200
	6-11 years	50	50	N/A
Fluticasone prop. (DPI)	12+ years	100-250	>250-500	>500
	6-11 years	50-100	>100-200	>200
Fluticasone prop. (MDI)	12+ years	100-250	>250-500	>500
	6-11 years	50-100	>100-200	>200
Mometasone (DPI)	12+ years	200	200	400
	6-11 years	N/A	N/A	N/A
Mometasone (MDI)	12+ years	200-400	200-400	>400
	6-11 years	100	100	200

ICS DAILY LOW DOSE CATEGORIZATION

IN CHILDREN AGES 5 YEARS AND YOUNGER

ICS (DELIVERY)	LOW TOTAL DAILY DOSE (MCG/DAY) (Age group with adequate safety & efficacy data)
Beclomethasone (MDI)	**50** (ages 5+ years)
Budesonide (nebulized)	**500** (ages 1+ years)
Ciclesonide (MDI)	**Not sufficiently studied in ages 5 and under**
Fluticasone furoate (DPI)	**Not sufficiently studied in ages 5 and under**
Fluticasone prop. (MDI)	**50** (ages 4+ years)
Mometasone (MDI)	**100** (ages 5+ years)

DPI: Dry-powder inhaler
MDI: Metered-dose inhaler

References: [1] 2024 GINA Report: Global Strategy for Asthma Management and Prevention; [2] FDA Prescribing Information for the individual medications.

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