DRUGS USED IN ASTHMA AND COPD

Asthma
- Asthma is a chronic inflammatory disease of the airways (interaction between many cells and inflammatory mediators).
- Inflammatory mediators are mast cells, eosinophils, T lymphocytes, neutrophils, epithelial cells, LTs, PGs and histamine.
- It is characterized by periodic attacks of wheezing, shortness of breath, chest tightness, and coughing.
- During very severe attacks, an asthma sufferer can turn blue from lack of oxygen, and can experience chest pain or even loss of consciousness. Severe asthma attacks may lead to respiratory arrest and death.

Epidemiology
- Asthma creates a clear burden on the patient relating to quality of life, but also on society in terms of emergency department (ED) visits, hospitalizations, and decreased productivity due to missed work and school.
- More than 27 million North Americans (300 million people worldwide) are affected with asthma.
- It is the most common chronic disease in American children. The highest percentage of prevalence is among children aged younger than 15 years especially boys. Adults and children miss most of the school days and work.
- Individuals aged 65 years and older represent the highest overall rate of death from asthma.

Risk Factors
- Precipitating factors are allergens (pollens, house dust, animal dander, mold, and cockroach), change in weather or season, exercise, hormonal change in women, irritants (tobacco smoke, air pollution), food, medications (aspirin, NSAIDs, nonselective BB), viral respiratory tract infection, and strong emotional expression (laughing or crying hard or stress).
- Current research suggests that genes coding various aspects of immune development are involved, and that there are numerous phenotypic expressions for these genes, each eliciting different inflammatory responses.
- Symptoms are often worse at nighttime or early in the morning and in the spring and fall when pollen levels are high.
- Gastroesophageal reflux disease (GERD), allergic rhinitis, obstructive sleep apnea, and obesity may also exacerbate asthma symptoms.

Diagnosis
- The medical history should address symptoms, pattern of symptoms (eg, time of day or season), specific triggers, family and social history, and history of exacerbations.
- Diagnosis and confirmation of asthma include peak flow measurement (FEV1), chest X ray, lung function tests, arterial blood gases and eosinophil count.
- Mucosal swelling, wheezing during normal breathing, and atopic dermatitis or eczema increase the probability of asthma.
- Signs of an asthmatic episode include wheezing, rapid breathing (tachypnea), prolonged expiration, a rapid heart rate (tachycardia), rhonchous lung sounds (audible through a stethoscope), and over-inflation of the chest.
Spirometry is an objective tool used to measure airflow limitation and establish the reversibility of airflow obstruction, an important feature that distinguishes asthma from other chronic respiratory diseases like chronic obstructive pulmonary disease (COPD).

- It measures the volume of air that can be forcibly blown out after maximal inhalation (forced vital capacity) and the volume of air that can be forcibly blown out in 1 second (forced expiratory volume in 1 second FEV₁).
- Measurements are taken before and after inhalation of a bronchodilator, and reversibility is determined by an increase in FEV₁ after its use.
- Normal FEV₁ value is 75% to 80% and is measured in volume in liters.

Pathophysiology

- Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role, in particular, mast cells, eosinophils, neutrophils, T lymphocytes, macrophages, and epithelial cells.
- In susceptible individuals, this inflammation causes recurrent episodes of coughing (particularly at night or early in the morning), wheezing, breathlessness, and chest tightness.
- These episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment.
- Airflow through the lungs is severely limited by inflammation, obstruction, hyper-responsiveness, and, eventually, airway remodeling. Inhaled allergens or irritants initiate an immunoglobulin E (IgE) response with activation of pro-inflammatory cells and mediators.
- Inflammation leads to leakage of plasma and cellular debris into the bronchial lumen, reduced mucus clearance, and formation of mucus plugs.
- While acute inflammation is a normal and beneficial response of tissues to injury, chronic inflammation leads to repeated repair of tissue with eventual scarring.
- Smooth muscle surrounding the bronchioles may be thickened and develop an exaggerated bronchoconstriction in response to stimuli that would have little or no effect in normal airways.
- Exacerbations of asthma are episodic, but underlying airway inflammation is continuously present.

Severity VS Control

- The Expert Panel Report recommends a stepwise approach to the treatment of asthma. An assessment of asthma severity is used to initiate therapy, whereas an assessment of asthma control is used to monitor and adjust therapy.
- Severity describes the underlying disease process and the extent of limitation to a patient's normal functioning.
- Control, on the other hand, is an assessment of how well therapeutic interventions have affected the clinical manifestations of the disease.
- An assessment of impairment and risk is initially used to classify asthma as intermittent, mild persistent, moderate persistent or severe persistent.
- Lung function is not a component of the severity assessment for children aged 0 to 4 years because of the inherent difficulty in attaining this measure.
- Asthma control is defined as symptoms and/or use of quick-relief medicines no more than twice a week, nighttime awakenings no more than twice a month, no interference with normal activities, and nearly normal lung function. If asthma is not well controlled, treatment should be stepped up by one step.
Daily use of quick-relief medications is a warning that asthma control is deteriorating and treatment should be reevaluated.

**Therapeutic Goals**
- Goals of therapy in asthma are to prevent chronic symptoms (coughing, breathlessness at night, early morning, after exertion), maintain near normal pulmonary function, physical activities, prevent recurrent hospitalization and provide optimal drug therapy with little or no adverse drug effects.

**COPD**
- It is a disease state characterize by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases.
- Cigarette smoking is the primary etiologic factor for the development of COPD.
- Chronic bronchitis is characterized by excessive mucus production and chronic productive cough is the hallmark.
- Emphysema is the complete alveolar destruction of lung walls.
- Influenza and pneumococcal vaccines annually are effective in patients with lung diseases in preventing COPD and asthma.
- Start with high dose and then step down therapy is preferred.

**Developing a patient – centered treatment plan**
- Developing a patient–provider relationship is at the core of effective asthma management.
- The discussion and development of goals should be a collaborative effort that uses the provider's recommendations and the patient's preferences to guide a personalized treatment plan.
- An asthma action plan helps a patient know what to do when his or her symptoms change or worsen.
- This plan should address each medication prescribed (both controller and quick-relief), symptoms that may occur with worsening control, changes in medications or doses if symptoms worsen, and whom to call in an emergency.
- Inhaler technique should be assessed at every visit. A patient may reasonably be using 2 or 3 different delivery devices for his controller and quick-relief medications.
- Many patients may benefit from using a valved holding chamber (ie, spacer) with their inhaler. The efficiency of drug delivery for an inhaled medication depends on proper administration, and pharmacists play a crucial role in ensuring that the patient understands the specific inhalation technique for each device.
- Patients should be educated on the differences between long-term control medications and quick-relief medications.
- Controller medications prevent symptoms and must be taken daily on a regular basis, not just when symptoms occur; they should not be used for quick relief during an asthma exacerbation.
- Rescue medications relax the airway smooth muscle to quickly increase airflow and relieve symptoms. They do not provide long-term control of asthma.

**Pharmacotherapy**
The Expert Panel Report recommends a stepwise approach to the treatment of asthma. Medication should be initiated based on an assessment of asthma severity and then stepped up if necessary and stepped down if possible based on asthma control.

When available, inhaled medications are preferred because they deliver a higher concentration of medication to the lungs with a much lower risk of systemic side effects.

The preferred therapy is similar among all age groups, but there have been very few studies of asthma treatment for young children, and many of the recommendations are extrapolated from data in older children and adults.

In 2 to 6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.

### Classifying Severity in Youths ≥ 12 Years and Adults

<table>
<thead>
<tr>
<th>Components of severity</th>
<th>Intermittent</th>
<th>Mild</th>
<th>Persistent</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impairment Normal FEV₁/FVC</td>
<td>Symptoms</td>
<td>≤ 2 days/week</td>
<td>≤ 2 days/week but not daily</td>
<td>Daily</td>
<td>Throughout the day</td>
</tr>
<tr>
<td>8 – 19 yr 85% 20 – 30 yr 80% 40 – 59 yr 75% 60 – 80 yr 70%</td>
<td>Nighttime Awakenings</td>
<td>≤ 2 times/month</td>
<td>3 – 4 times/month</td>
<td>&gt; 1 time/week but not nightly</td>
<td>Often 7 times/week</td>
</tr>
<tr>
<td></td>
<td>SABA use for symptoms control</td>
<td>≤ 2 days/week</td>
<td>&gt; 2 days/week but not daily and not more than 1 time on any day</td>
<td>Daily</td>
<td>Several times per day</td>
</tr>
<tr>
<td></td>
<td>Interference with normal activity</td>
<td>None</td>
<td>Minor Limitation</td>
<td>Some limitation</td>
<td>Extremely limited</td>
</tr>
<tr>
<td></td>
<td>Lung function</td>
<td>Normal FEV₁ between exacerbations</td>
<td>FEV₁ &gt; 80% predicted FEV₁/FVC normal</td>
<td>FEV₁ &gt; 60% but &lt; 80% predicted</td>
<td>FEV₁ &lt; 60% predicted FEV₁/FVC reduced &gt; 5%</td>
</tr>
<tr>
<td>Risk</td>
<td>Exacerbations requiring Oral systemic corticosteroids</td>
<td>0 – 1 per year</td>
<td>≥ 2 per year</td>
<td>Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category.</td>
<td></td>
</tr>
</tbody>
</table>

### Recommended step for Initiating Treatment

- **Step 1**
- **Step 2**
- **Step 3** (± PO systemic corticosteroids)
- **Step 4 or 5** (± PO systemic corticosteroids)
### STEPWISE APPROACH TO TREATMENT IN YOUTHS ≥ 12 YEARS OF AGE AND ADULTS

<table>
<thead>
<tr>
<th>Intermittent</th>
<th>Persistent Daily Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step 1</strong></td>
<td><strong>Step 2</strong></td>
</tr>
<tr>
<td>SABA PRN</td>
<td>Preferred: Low dose ICS</td>
</tr>
<tr>
<td></td>
<td>Alternative: Cromolyn, LTRA, Nedocromil, Theophylline</td>
</tr>
<tr>
<td></td>
<td><strong>Step 3</strong></td>
</tr>
<tr>
<td></td>
<td>Preferred: Low dose ICS + LABA or medium – dose ICS</td>
</tr>
<tr>
<td></td>
<td>Alternative: Low dose ICS + either LTRA, theophylline or zileuton</td>
</tr>
<tr>
<td></td>
<td><strong>Step 4</strong></td>
</tr>
<tr>
<td></td>
<td>Preferred: Medium dose ICS + LABA</td>
</tr>
<tr>
<td></td>
<td>Alternative: medium dose ICS + either LTRA, theophylline or zileuton</td>
</tr>
<tr>
<td></td>
<td><strong>Step 5</strong></td>
</tr>
<tr>
<td></td>
<td>High dose ICS + LABA and consider omalizumab</td>
</tr>
<tr>
<td></td>
<td>High dose ICS + LABA + oral corticosteroids and consider omalizumab</td>
</tr>
<tr>
<td></td>
<td><strong>Step 6</strong></td>
</tr>
<tr>
<td></td>
<td>High dose ICS + LABA + oral corticosteroids and consider omalizumab</td>
</tr>
</tbody>
</table>

### β₂ Agonists (SABA and LABA)

- Quick-relief medications should be provided at all steps of treatment.
- Short acting beta₂ - agonists are the preferred choice for relief of acute symptoms.
- They relax the smooth muscle surrounding the airways, providing symptom relief within 3 to 5 minutes.
- Patients may use up to 3 treatments at 20 - minute intervals depending on the severity of their symptoms.
- Nonselective inhaled beta₂ - agonists (eg, epinephrine, isoproterenol, metaproterenol) are not recommended because their beta1 activity can increase cardiovascular side effects.
- A 2 week trial period is necessary before increasing or changing the drug.
- A short-acting anticholinergic (ipratropium) is occasionally used in EDs because it provides an additive benefit to SABAs in moderate-to-severe exacerbations.
- Ipratropium may be considered as the primary reliever medication in patients who do not tolerate SABAs.
- Tiotropium, a long acting anticholinergic, is not approved for asthma.
- Use with corticosteroids provides improve symptoms and ↓ incidence of exacerbation.
- Inhaled long-acting beta₂ - agonists have the same, mechanism of action as SABAs, but with a duration of effect of at least 12 hours, which allows for twice-daily administration.
- Adding an LABA to low-dose ICSs improves multiple domains of asthma control more than doubling the dose of the ICS and spares dose-dependent side effects of glucocorticoids.
- For this reason, they are the preferred add-on therapy to ICSs.
# SABA

<table>
<thead>
<tr>
<th>Name</th>
<th>Dose, Efficacy and Indications</th>
<th>Adverse effects</th>
<th>Interactions/Precautions/Monitoring/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albuterol/Salbutamol (Ventolin, Proair, Airomir)</td>
<td>Ventolin/Proair/Airomir/Fenoterol (100 mcg puff/actuation): 1 to 2 puffs qid prn (max of 8 puffs/day) Terbutaline (0.5 mg/puff): 1 puff q 4 to 6 h prn (max of 6 puffs/day)</td>
<td>Beta₂ mediated are Tremor Palpitations Restlessness Nervousness Hypokalemia Wakefulness hyperglycemia Hypotension</td>
<td>Short acting are safe in pregnancy Shake well MDIs before use and prime <strong>Wait at least one minute before inhaling the next puff of medicine</strong> Exhale slowly Monitor FEV₁, peak flow, pulmonary function tests, blood pressure and heart rate Increase use of short acting beta agonist means deterioration of asthma condition. MAOIs, TCAs, diuretics and digoxin. Formeterol is rapid acting and can be used as rescue therapy.</td>
</tr>
</tbody>
</table>

# LABA

<table>
<thead>
<tr>
<th>Name</th>
<th>Dose, Efficacy and Indications</th>
<th>Adverse effects</th>
<th>Interactions/Precautions/Monitoring/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formeterol (Oxeze/Foradil)</td>
<td>Oxeze Tubuhaler: 6 – 12 mcg q 12 h (max of 4 mcg/day) Foradil (12 mcg/capsule): Inhalte contents of 1 capsule BID, max of 48 mcg/d Serevent Diskhaler (50mcg/puff): 1 puff BID</td>
<td>Beta₂ mediated are Tachycardia</td>
<td></td>
</tr>
<tr>
<td>Salmeterol (Serevent)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Anticholinergics

<table>
<thead>
<tr>
<th>Name</th>
<th>Dose, Efficacy and Indications</th>
<th>Adverse effects</th>
<th>Interactions/Precautions/Monitoring/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipratropium Br (Atrovent), 20 mcg/puff 2 – 4 puffs q 6 – 8 hr prn Tiotropium, Caps (spiriva) 1 spiriva inhalation daily</td>
<td>Muscarinic receptors blocker Ipratropium acts in lungs, especially larger airways and doesn’t dry out airway obstruction. <strong>Blocks ACh, reduces cholinergic tone and produce bronchodilation</strong> <strong>ASTHMA:</strong> Limited efficacy Not protective VS early/late responses or exercised induced <strong>COPD:</strong> First line agent High dose acceptable if tolerable</td>
<td>Dry mouth Metallic taste Blurred vision</td>
<td>Shake well MDIs before use and prime <strong>Wait at least one minute before inhaling the next puff of medicine</strong> Exhale slowly Avoid contact with eyes Spiriva capsules are intended for use in the inhaler provided. <strong>Do not swallow the capsules.</strong> Do not use the inhaler device to administer any medication other than Spiriva. If monotherapy does not reach goal, may add 2nd agent and if goal still not met, add 3rd agent and if no significant improvement then discontinue treatment. Benefits maintained with continued therapy</td>
</tr>
</tbody>
</table>
Inhaled Corticosteroids (ICS)

- ICSs are the **preferred long-term control** medication for initiating therapy in all age groups and at all steps of therapy. They target the primary pathophysiologic manifestation of asthma-chronic inflammation.
- Most of the benefit is seen in the low- to medium- dose range, but because of the variability in response among patients, higher doses are often needed.
- Add - on therapy with a medication from another class is often preferred over increasing the dose of ICSs in order to minimize side effects.
- Once a patient has maintained asthma control for 3 months, a **dose reduction by 25% to 50% in the ICS** should be considered.

<table>
<thead>
<tr>
<th>Name and Dosing</th>
<th>Efficacy and Indications</th>
<th>Adverse effects</th>
<th>Interactions/Precautions/Monitoring/Comments</th>
</tr>
</thead>
</table>
| **Beclomethasone**  
(Qvar, Vanceril, Beconase) | Anti-inflammatory  
Increase number of $\beta_2$ receptors  
Reduce mucus production/secretion  
**ASThma:** Turbohaler delivers twice the dose VS MDI.  
**COPD:** Approx 20% patient respond  
**Can increase FEV$_1$ by 20% in those which respond** | Sore throat  
Sore mouth  
**Oral thrush**  
Dysphonia  
Hoarseness  
**Long Term, dose Dependent**  
Hyperglycemia, potassium loss  
Cushing syndrome  
Adrenal suppression  
**Osteoporosis**  
Cataract  
Decrease immune system  
Muscle weakness | Oral thrush can be reduced by rinsing mouth or using spacer  
**If using bronchodilator and steroid then use bronchodilator first and use bronchodilator after few minutes.**  
Absorption from lungs in most likely contributor to possible HPA suppression of other systemic effects.  
Delivery system affects pulmonary system.  
**Addition of spacer also increases pulmonary deposition.**  
Low dosages are accepted as quite safe.  
Favor **starting at high and stepping down.**  
Patient education may have greater effectiveness.  
Administration of ICS is **preferred BID.**  
**More than 3 – 4 puffs at each dosing should be avoided.**  
Compliance is major determinant of success with aerosol corticosteroids and education is essential. |
| **Budesonide**  
(Pulmicort) | **Use for acute exacerbations (oral)**  
QVAR: 200 – 2000 mcg/d BID – QID in divided dose | |
| **Fluticasone**  
(Flovent, Flovent HFA) | Turbohaler delivers twice the dose VS MDI.  
**COPD:** | |
| **Ciclesonide**  
(Alvesco) | **Use for acute exacerbations (oral)**  
QVAR: 200 – 2000 mcg/d BID – QID in divided dose | |
| **Mometasone**  
(Asmanex)  
110/220 mcg/actuation | | |
| **Triamcinolone**  
(Azmacort)  
75 mcg/actuation | | |
Fluticasone/Salmetarol
(Advair Diskus)
100/50, 250/50, 500/50

Asthma maintenance for patients 4 – 11 years: use, 100/50 mcg INH bid for pts not controlled on inhaled steroid
Adults: 100/50-250/50 mcg INH bid if not on inhaled steroid.
COPD adults: 250/50 mcg INH bid

Upper respiratory infection
Pharyngitis
Dysphonia
Candidiasis

RISK ASTHMA RELATED DEATHS
Avoid with phenothiazine, beta 2 agonists, and sotalol
Indicated for the long-term, twice-daily, maintenance treatment of asthma in patients 4 years of age and older.
Contraindicated in asthmatics.
Do not use a spacer device with Advair Diskus.

Chromoglycates

<table>
<thead>
<tr>
<th>Name and Dosing</th>
<th>Efficacy and Indications</th>
<th>Adverse effects</th>
<th>Interactions/Precautions/Monitoring/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cromolyn (Intal) 1 mg/puff 2 puffs QID</td>
<td>Mast cell stabilizers ASTHMA: Inhibits early/late response and exercise induced asthma Effective prophylactically in children with mild to moderate asthma Must be used regularly in order to provide significant protection</td>
<td>Rare</td>
<td>Nedocromil is an effective anti-inflammatory agent, especially for mild persistent asthma and is similar to cromolyn in efficacy and in low incidence of side effects.</td>
</tr>
<tr>
<td>Nedocromil (Tilade) 2 mg/puff 4 puffs QID</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Theophyllines

- Sustained - release theophylline is the most commonly used methylxanthine.
- It is a nonselective phosphodiesterase inhibitor with bronchodilator and modest anti-inflammatory activity.
- It is generally considered an alternative, not preferred, monotherapy or add-on therapy in patients 5 years of age and older with persistent asthma and it is not recommended at any step of therapy for children younger than 5 years of age.
- Its use is limited by its side effects.
- Patients should have a trial of 2 – 4 weeks to find out efficacy. If no improvement discontinue therapy.
<table>
<thead>
<tr>
<th>Name and Dosing</th>
<th>Efficacy and Indications</th>
<th>Adverse effects</th>
<th>Interactions/Precautions/Monitoring/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Theophylline</td>
<td>Inhibit phosphodiesterase activity and increase cAMP</td>
<td>Nausea, Nervousness</td>
<td>Increases levels of Cimetidine, erythromycin, verapamil, quinolones, fluvoxamine</td>
</tr>
<tr>
<td>(Theodur, uniphyl) Caps, elixir</td>
<td>Mild anti-inflammatory activity</td>
<td>Headache</td>
<td>Decreases levels of Rifampin, Carbamazepine, Phenytoin, Smoking</td>
</tr>
<tr>
<td>Soln, Tab, Inj</td>
<td>Theophylline anhydrous oral solid form contains 100% theophylline content</td>
<td>Signs of toxicity</td>
<td>Contraindicated in CHF</td>
</tr>
<tr>
<td>200 – 300 mg po BID in divided dose</td>
<td>Theophylline monohydrate oral solution contains 91% theophylline content</td>
<td>Vomiting, Palpitations, Tremor, Seizures hypokalemia</td>
<td>Liver disease decrease theophylline clearance</td>
</tr>
<tr>
<td>Aminophylline</td>
<td>ASTHMA: Not for early response</td>
<td></td>
<td>Theophylline LA oral preparation should be taken with full glass of water, swallowed whole or cut into half if scored, do not crush.</td>
</tr>
<tr>
<td>(Phyllocontin) Inj, Liq, tabs</td>
<td>Not first line</td>
<td></td>
<td>Monitor heart rate, CNS effects and respiratory rate</td>
</tr>
<tr>
<td>225 – 350 mg po BID</td>
<td>Improves FEV₁ and dyspnea</td>
<td></td>
<td>Aminophylline injection contains 79 – 88% theophylline content</td>
</tr>
<tr>
<td></td>
<td>Improve respiratory muscle fatigue, mucociliary clearance, and gas exchange</td>
<td></td>
<td>Therapeutic levels are 10 – 20 mcg/ml and adverse reactions are noticed when serum concentration is 25 mcg/ml.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Levels &gt; than 35mcg/ml are fatal</td>
</tr>
</tbody>
</table>

**Antileukotrienes Modifiers**

- This therapeutic class includes leukotriene receptor antagonists (montelukast, zafirlukast) and a 5 - lipoxygenase inhibitor (zileuton).
- **Montelukast is the only leukotriene modifier approved for children younger than 5 years**, and recommendation for its use as add - on therapy to ICSs in this population is equal to that of an LABA in steps 4 to 6.
- Zafirlukast is approved for adults and children 5 years and older and is recommended as an alternative therapy for persistent asthma.
<table>
<thead>
<tr>
<th>Name and Dosing</th>
<th>Efficacy and Indications</th>
<th>Adverse effects</th>
<th>Interactions/Precautions/Monitoring/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zafirlukast, (Accolate) tabs 20 mg po BID</td>
<td>Selective cysteinyl leukotriene receptor antagonist anti-inflammatory effects Zileuton blocks 5 lipooxygenase ASTHMA: Early response and exercise When steroids can’t be use and ASA induced asthma Determine 6 – 8 week trial to see effects</td>
<td>N/D and abdominal pain Headache</td>
<td>Take zafirlukast on empty stomach 1 hr before or 2 hr after meals children 2 – 5 years can take one 4 mg chewable tab of montelukast q hs or evening time children 6 – 14 years can take one 5 mg chewable tab q hs Zileuton is contraindicated in hepatic impairment Monitor closely in patients who consume large quantities of alcohol. Monteleukast has been shown to result in reduction of ICS dose. Zileuton requires 4 daily dosing and has more side effects and drug interactions.</td>
</tr>
<tr>
<td>Monelukast, (Singular) tabs. 10 mg po HS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zileuton, (Zyflo) tab 600 mg po QID with food HS</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Systemic Corticosteroids**
- Systemic corticosteroids (dexamethasone, hydrocortisone, methylprednisolone, prednisolone, and prednisone) are used for moderate- to-severe exacerbations, because they speed resolution of symptoms and prevent recurrent exacerbations.
- Onset of anti-inflammatory activity occurs within 4 to 6 hours, and treatment should continue for 5 to 10 days depending on the severity of the exacerbation.
- Possible side effects include (but are not limited to) hyperglycemia, increased appetite, fluid retention, weight gain, changes in mood, and peptic ulcer. Refer to the section on inhaled corticosteroids (ICSs) for a discussion of potential long-term effects of glucocorticoids.

**Immunomodulators**
- Omalizumab (Xolair) is a monoclonal antibody that prevents IgE from binding to basophils and mast cells.
- Its only indication is as adjunctive therapy in patients with severe allergic asthma who are not controlled on ICSs.
- It is administered by subcutaneous injection every 2 to 4 weeks, with the dose depending on serum IgE levels and the patient's body weight.
- Omalizumab has been shown to increase quality of life and decrease severe exacerbations and ED visits in patients already taking high-dose ICSs plus and LABA.

**Metered Dose Inhaler (MDI):** is aerosol canister with actuation device valve that controls precise release of a premeasured amount. Drug in the canister is a suspension or solution mixed with propellant.
Air Jet Nebulizer: Drug is placed in a small volume of solute and placed in a small reservoir (nebulizer) connected to an air source such as small compressor pump and an oxygen tank. Air travels from the relatively large diameter tubing of the air source into a pinhole–sized opening in the nebulizer, creating a negative pressure at the site of entry and causes the drug solution in the solution in the bottom of the nebulizer reservoir to be sucked up through a small capillary tube where it then encounters the rapid airflow. Drug solution is forced against a small baffle that causes mechanical formation of a mist.

Diskus: Hold the diskus in one hand and put the thumb of your other hand on the thumb grip. Push your thumb away from you as far as it will go until the mouthpiece appears and snaps into position. Hold the diskus in a level, flat position with the mouthpiece towards you. Slide the lever away from you as far as it will go until it clicks. It is ready to use. Every time the lever is pushed back, a dose is ready to be inhaled. This is shown by a decrease in numbers on the dose counter. Before inhaling your dose from the diskus, breathe out (exhale) fully while holding the diskus level and away from your mouth. Never breathe out into the diskus mouthpiece. Put the mouthpiece to your lips. Breathe in quickly and deeply through the diskus. Remove the diskus from your mouth. Hold your breath for about 10 seconds, or for as long as is comfortable. Breathe out slowly. Never wash the mouthpiece or any part of the diskus. Keep it dry. Rinse your mouth with water after breathing-in the medicine. Spit the water out. Do not swallow.