Back to Basics: Pediatric Asthma Pharmacology
Marie Backus, PharmD
Objectives

• Understand how medications used in the treatment of asthma work to prevent or treat symptoms.
• Recognize common side effects of medications used in the treatment of asthma.
• Be able to describe how to use a prescribed medication.
Asthma

• Estimated to effect at least 22 million Americans
• One of the most common chronic diseases of childhood

• Characteristics
  o Airway Inflammation
  o Bronchoconstriction
  o Hyperresponsiveness
  o Edema
Diagnosis

• Recurrent episodes of airflow obstruction or hyperresponsiveness
  o Medical history and physical exam
    • Wheezing (recurrent)
    • Cough (worse at night)
    • Difficulty breathing (recurrent)
    • Chest tightness (recurrent)
  • Triggers that cause symptoms or make symptoms worse
    o Exercise
    o Viral infection
    o Allergens (fur, dust mites, mold, pollen)
    o Irritants (smoke)
    o Weather changes
    o Laughing or crying hard
    o Stress
    o Menstrual cycles
Diagnosis

• Airflow obstruction is reversible
  o Response to short acting beta$_2$-agonist (albuterol)
  o Spirometry: FEV$_1$ increase more than 200 ml and at least 12% increase from baseline

• Alternate diagnosis excluded
  o Allergic rhinitis/sinusitis, Vocal cord dysfunction, foreign body, bronchiolitis, cystic fibrosis, laryngotracheomalacia, aspiration from swallowing dysfunction or gastroesophageal reflux
Treatment Goals

• Prevent symptoms
• Require symptom relief with SABA less than 2 times a week
• Prevent recurrent exacerbations
• Maintain normal pulmonary function
• Prevent loss of lung function
• Maintain normal activity levels
• Provide optimal pharmacotherapy with minimal adverse effects
Classifying Asthma

• Severity (to initiate therapy)
  o Intermittent
  o Mild Persistent
  o Moderate Persistent
  o Severe Persistent

• Based on
  o Frequency of symptoms
  o Frequency of nighttime awakenings
  o Frequency of short-acting beta$_2$ agonist use for symptom control
  o Interference with normal activity
  o Lung function (5 years and older)

• After treatment is started, assess level of control based on parameters listed above (to adjust therapy)
  o Well controlled, not well controlled, very poorly controlled
### Components of Severity

<table>
<thead>
<tr>
<th>Impairment</th>
<th>Intermittent</th>
<th>Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ages 0-4</td>
<td>Ages 5-11</td>
</tr>
<tr>
<td>Symptoms</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week but not daily</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>0</td>
<td>≤2x/month</td>
</tr>
<tr>
<td>Short-acting beta-agonist use for symptom control</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week but not daily</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
<td>Minor limitation</td>
</tr>
<tr>
<td>Lung Function</td>
<td>Normal FEV₁ between exacerbations</td>
<td>&gt;80%</td>
</tr>
<tr>
<td>• FEV₁ (predicted) or peak flow (personal best)</td>
<td>&gt;85%</td>
<td>&gt;80%</td>
</tr>
<tr>
<td>Risk</td>
<td>Exacerbations requiring oral systemic corticosteroids (consider severity and interval since last exacerbation)</td>
<td>0-1/year (see notes)</td>
</tr>
</tbody>
</table>

### Recommended Step for Initiating Therapy

(See "Stepwise Approach for Managing Asthma" for treatment steps.)

The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.

#### Step 1
(for both age groups)

#### Step 2
(for both age groups)

#### Step 3 and consider short course of oral systemic corticosteroids

#### Step 3: medium-dose ICS option OR step 4 and consider short course of oral systemic corticosteroids

In 2-6 weeks, depending on severity, evaluate level of asthma control that is achieved.

- Children 0-4 years old: If no clear benefit is observed in 4-6 weeks, stop treatment and consider alternative diagnoses or adjusting therapy.
- Children 5-11 years old: Adjust therapy accordingly.
## Classification of Asthma Severity

**≥12 years of age**

<table>
<thead>
<tr>
<th>Components of Severity</th>
<th>Persistent</th>
<th>Intermittent</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Impairment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal FEV₁/FVC:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8–19 yr</td>
<td>85%</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week but not daily</td>
<td>Daily</td>
<td>Throughout the day</td>
</tr>
<tr>
<td>20–39 yr</td>
<td>80%</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week but not daily</td>
<td>Daily</td>
<td>Often 7x/week</td>
</tr>
<tr>
<td>40–59 yr</td>
<td>75%</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week but not daily, and not more than 1x on any day</td>
<td>Daily</td>
<td>Several times per day</td>
</tr>
<tr>
<td>60–80 yr</td>
<td>70%</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week but not daily, and not more than 1x on any day</td>
<td>Daily</td>
<td>Several times per day</td>
</tr>
<tr>
<td><strong>Lung function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptoms</td>
<td>None</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week but not daily</td>
<td>Daily</td>
<td>Throughout the day</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>≤2x/month</td>
<td>3–4x/month</td>
<td>&gt;1x/week but not nightly</td>
<td>Often 7x/week</td>
<td></td>
</tr>
<tr>
<td>Short-acting beta₂-agonist use for symptom control (not prevention of EIB)</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week but not daily, and not more than 1x on any day</td>
<td>Daily</td>
<td>Several times per day</td>
<td></td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
<td>Minor limitation</td>
<td>Some limitation</td>
<td>Extremely limited</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Exacerbations</strong></td>
<td></td>
<td>0–1/year (see note)</td>
<td>≥2/year (see note)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral systemic corticosteroids</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Relative annual risk of exacerbations may be related to FEV₁.</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Recommended Step for Initiating Treatment

(See “Stepwise Approach for Managing Asthma” for treatment steps.)

- **Step 1**
- **Step 2**
- **Step 3**
- **Step 4 or 5**

In 2–6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.
### Components of Control

#### Assessing Asthma Control and Adjusting Therapy in Children

<table>
<thead>
<tr>
<th></th>
<th>Well Controlled</th>
<th>Not Well Controlled</th>
<th>Very Poorly Controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ages 0–4</strong></td>
<td><strong>Ages 5–11</strong></td>
<td><strong>Ages 0–4</strong></td>
<td><strong>Ages 5–11</strong></td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td>≤2 days/week but not more than one on each day</td>
<td>&gt;2 days/week or multiple times on ≤2 days/week</td>
<td>Throughout the day</td>
</tr>
<tr>
<td><strong>Nighttime awakenings</strong></td>
<td>≤1/wk/month</td>
<td>&gt;1/wk/month</td>
<td>&gt;1/wk/month</td>
</tr>
<tr>
<td><strong>Interference with normal activity</strong></td>
<td>None</td>
<td>Some limitation</td>
<td>Extremely limited</td>
</tr>
<tr>
<td><strong>Short-acting beta2-agonist use for symptom control (not prevention of EIB)</strong></td>
<td>≤2 days/week</td>
<td>&gt;2 days/week</td>
<td>Several times per day</td>
</tr>
<tr>
<td><strong>Lung function</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- FEV1 (predicted) or peak flow personal best</td>
<td>N/A</td>
<td>&gt;80%</td>
<td>N/A</td>
</tr>
<tr>
<td>- FEV1/FVC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Exacerbations requiring oral systemic corticosteroids</strong></td>
<td>0–1 x/year</td>
<td>2–3 x/year</td>
<td>&gt;3 x/year</td>
</tr>
<tr>
<td><strong>Reduction in lung growth</strong></td>
<td>N/A</td>
<td>Requires long-term followup</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Treatment-related adverse effects</strong></td>
<td>Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Recommended Action for Treatment

**(See “Stepwise Approach for Managing Asthma” for treatment steps.)**

The stepwise approach is meant to assist, not replace, clinical decisionmaking required to meet individual patient needs.

- Maintain current step.
- Regular followup every 1–6 months.
- Consider step down if well controlled for at least 3 months.

- **Step up 1 step**
- **Step up at least 1 step**
- **Consider short course of oral systemic corticosteroids,**
  **Step up 1–2 steps**

- **Before step up:**
  - Review adherence to medication, inhaler technique, and environmental control.
  - If alternative treatment was used, discontinue it and use preferred treatment for that step.
  - Reevaluate the level of asthma control in 2–6 weeks to achieve control; every 1–6 months to maintain control.

  **Children 0–4 years old:** If no clear benefit is observed in 4–6 weeks, consider alternative diagnoses or adjusting therapy.
  **Children 5–11 years old:** Adjust therapy accordingly.

- For side effects, consider alternative treatment options.
## Classification of Asthma Control

### Components of Control

<table>
<thead>
<tr>
<th>Impairment</th>
<th>Well Controlled</th>
<th>Not Well Controlled</th>
<th>Very Poorly Controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week</td>
<td>Throughout the day</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>≤2x/month</td>
<td>1–3x/week</td>
<td>≥4x/week</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
<td>Some limitation</td>
<td>Extremely limited</td>
</tr>
<tr>
<td>Short-acting beta₂-agonist use for symptom control (not prevention of EIB)</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week</td>
<td>Several times per day</td>
</tr>
<tr>
<td>FEV₁ or peak flow</td>
<td>&gt;80% predicted/personal best</td>
<td>60–80% predicted/personal best</td>
<td>&lt;60% predicted/personal best</td>
</tr>
<tr>
<td>Validated questionnaires</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATAQ</td>
<td>0</td>
<td>1–2</td>
<td>3–4</td>
</tr>
<tr>
<td>ACQ</td>
<td>≤0.75*</td>
<td>≥1.5</td>
<td>N/A</td>
</tr>
<tr>
<td>ACT</td>
<td>≥20</td>
<td>16–19</td>
<td>≤15</td>
</tr>
<tr>
<td>Exacerbations requiring oral systemic corticosteroids</td>
<td>0–1/year</td>
<td>≥2/year (see note)</td>
<td></td>
</tr>
<tr>
<td>Risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progressive loss of lung function</td>
<td>Evaluation requires long-term followup care.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment-related adverse effects</td>
<td>Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Recommended Action for Treatment

(See “Stepwise Approach for Managing Asthma” for treatment steps.)

- **Well Controlled**: Maintain current step. Regular followup at every 1–6 months to maintain control. Consider step down if well controlled for at least 3 months.
- **Not Well Controlled**: Step up 1 step. Reevaluate in 2–6 weeks. For side effects, consider alternative treatment options.
- **Very Poorly Controlled**: Consider short course of oral systemic corticosteroids. Step up 1–2 steps. Reevaluate in 2 weeks. For side effects, consider alternative treatment options.
### Step 1

**Interruption Asthma**
- **Preferred**: SABA PRN
- **Alternative**: Cromolyn or Montelukast

**Persistent Asthma: Daily Medication**
- **Consult with asthma specialist if step 3 care or higher is required. Consider consultation at step 2.**
- **Preferred**: Low-dose ICS
- **Alternative**: Cromolyn or Montelukast

### Each Step: Patient Education and Environmental Control

**Quick-Relief Medication**
- **SABA** as needed for symptoms. Intensity of treatment depends on severity of symptoms.
- **With viral respiratory symptoms**: SABA q 4–6 hours up to 24 hours (longer with physician consult). Consider short course of oral systemic corticosteroids if exacerbation is severe or patient has history of previous severe exacerbations.

**Caution**: Frequent use of SABA may indicate the need to step up treatment. See text for recommendations on initiating daily long-term-control therapy.

### Step 2

**Interruption Asthma**
- **Preferred**: SABA PRN
- **Alternative**: Cromolyn, LTRA, Nedocromil, or Theophylline

**Persistent Asthma: Daily Medication**
- **Consult with asthma specialist if step 4 care or higher is required. Consider consultation at step 3.**
- **Preferred**: Low-dose ICS + LABA, LTRA, or Theophylline OR
- **Alternative**: Medium-dose ICS + LABA, LTRA, or Theophylline

### Step 3

**Each Step: Patient Education, Environmental Control, and Management of Comorbidities**

**Steps 2–4:** Consider subcutaneous allergen immunotherapy for patients who have persistent, allergic asthma.

**Quick-Relief Medication**
- **SABA** as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.

**Caution**: Increasing use of SABA or use >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.

### Step 4

**Interruption Asthma**
- **Preferred**: SABA PRN
- **Alternative**: Cromolyn, LTRA, Nedocromil, or Theophylline

**Persistent Asthma: Daily Medication**
- **Preferred**: Low-dose ICS + LABA, LTRA, or Theophylline
- **Alternative**: Medium-dose ICS + LABA, LTRA, or Theophylline

### Step 5

**Interruption Asthma**
- **Preferred**: SABA PRN
- **Alternative**: Cromolyn, LTRA, Nedocromil, or Theophylline

**Persistent Asthma: Daily Medication**
- **Preferred**: Low-dose ICS + LABA, LTRA, or Theophylline
- **Alternative**: Medium-dose ICS + LABA, LTRA, or Theophylline

### Step 6

**Interruption Asthma**
- **Preferred**: SABA PRN
- **Alternative**: Cromolyn, LTRA, Nedocromil, or Theophylline

**Persistent Asthma: Daily Medication**
- **Preferred**: Low-dose ICS + LABA, LTRA, or Theophylline
- **Alternative**: Medium-dose ICS + LABA, LTRA, or Theophylline

---

**Notes:**
- Assess control.
- Step down if possible and asthma is well controlled at least 3 months.
- Step up if needed (first check inhaler technique, adherence, environmental control, and comorbid conditions).
Intermittent Asthma
Consult with asthma specialist if step 4 care or higher is required.
Consider consultation at step 3.

Step 1
Preferred: Low-dose ICS
Alternative: Cromolyn, LTRA, Nedocromil, or Theophylline

Step 2
Preferred: Low-dose ICS + LABA
OR Medium-dose ICS
Alternative: Low-dose ICS + either LTRA, Theophylline, or Zileuton

Step 3
Preferred: Medium-dose ICS + LABA
AND Consider Omalizumab for patients who have allergies

Step 4
Preferred: High-dose ICS + LABA
AND Consider Omalizumab for patients who have allergies

Step 5
Preferred: High-dose ICS + LABA
AND Consider Omalizumab for patients who have allergies

Step 6
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)

Each step: Patient education, environmental control, and management of comorbidities.
Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).

Quick-Relief Medication for All Patients
- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Low Daily Dose</th>
<th>Medium Daily Dose</th>
<th>High Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Child 0–4 Years of Age</td>
<td>Child 5–11 Years of Age</td>
<td>≥12 Years of Age and Adults</td>
</tr>
<tr>
<td><strong>Beclohexazole HFA</strong></td>
<td>NA</td>
<td>80–160 mcg</td>
<td>80–240 mcg</td>
</tr>
<tr>
<td>40 or 80 mcg/puff</td>
<td>NA</td>
<td>180–400 mcg</td>
<td>180–600 mcg</td>
</tr>
<tr>
<td><strong>Budesonide DPI</strong></td>
<td>NA</td>
<td>0.5 mg</td>
<td>NA</td>
</tr>
<tr>
<td>90, 180, or 200 mcg/ inhalation</td>
<td>0.25–0.5 mg</td>
<td>0.5 mg</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Budesonide Inhaled Inhalation suspension for nebulization</strong></td>
<td>176 mcg</td>
<td>88–176 mcg</td>
<td>88–264 mcg</td>
</tr>
<tr>
<td><strong>Fluticasone</strong></td>
<td>NA</td>
<td>100–200 mcg</td>
<td>100–300 mcg</td>
</tr>
<tr>
<td><strong>DPI: 50, 100, or 250 mcg/ inhalation</strong></td>
<td>NA</td>
<td>100–200 mcg</td>
<td>100–300 mcg</td>
</tr>
<tr>
<td><strong>Mometasone DPI</strong></td>
<td>NA</td>
<td>200 mcg</td>
<td>NA</td>
</tr>
<tr>
<td>200 mcg/ inhalation</td>
<td>NA</td>
<td>200 mcg</td>
<td>NA</td>
</tr>
</tbody>
</table>
Quick-relief medications

• Short acting beta$_2$ agonists (SABA)
  o Albuterol
  o Levalbuterol

• Anticholinergics
  o Ipratropium bromide
Short acting beta$_2$ agonists (SABA)

- Albuterol and Levalbuterol
- Use: relief of acute symptoms; drug of choice for acute asthma symptoms and exacerbations
- MOA: bronchodilation; relax airway smooth muscle by binding to beta$_2$ receptors. Increase in airflow within 3 to 5 minutes.

- Frequency of use
  - Using more than twice a week for symptom relief is a sign of uncontrolled asthma
  - Using more than one inhaler a month (200 puffs) may be a sign of inadequate control
    - Associated with an increased risk of acute exacerbation that requires ED or hospitalization
SABA Dosing

- **Albuterol**
  - **Inhaler:** 2-4 puffs every 4 to 6 hours as needed
    - Acute exacerbation: 2 to 6 puffs every 20 mins x 3 doses, then every 3 to 4 hours for 24 to 48 hours
    - EIB: 2 puffs 5 minutes before exercise
  - **Nebulization solution:** 1.25 to 5 mg every 4 to 8 hours as needed
    - Hospital: 2.5 mg every 20 mins x 3 doses or continuous 10 to 20 mg/hr

- **Levalbuterol**
  - **Inhaler:** 2 puffs every 4 to 6 hours as needed
    - Acute exacerbation: 4 to 8 puffs every 20 mins x 3 doses, then every 1 to 4 hours
  - **Nebulization solution:** 0.31 to 1.25 mg every 4 to 8 hours as needed
    - Acute exacerbation: 1.25 to 2.5 mg every 20 mins x 3 doses, then every 1 to 4 hours

- **Side effects:**
  - Tachycardia, excitement, nervousness, muscle tremor, hypokalemia, hyperglycemia
SABA Inhalers

Inhalation Aerosols

Inhalation Powder
Metered-Dose Inhaler (MDI) Technique

- Prime inhaler (if needed)
  - Proair and generic: first use or not used for more than 2 weeks (3 sprays)
  - Ventolin and Proventil: first use or not used for more than 2 weeks (4 sprays)
  - Xopenex: first use and if not used for more than 3 days (4 sprays)

- Remove cap and shake inhaler

- Stand or sit up straight and breath out completely

- Put the mouthpiece in your mouth and close your lips around it

- As you start to breath in slowly, press the inhaler one time

- Breath in slowly and deeply then hold your breath while counting slowly to 10 or as long as you are able

- Repeat doing one puff at a time, waiting 15 to 30 seconds between puffs

- Cleaning: at least weekly wash actuator with warm running water for 30 seconds, shake off excess, air dry (remove canister)
Valved Holding Chamber (VHC) / Spacer

• Pros:
  o Ideal for patients who have difficulty MDI technique
    • One way valve does not allow patient to exhale into device
    • Patient can breath normally to receive medication
    • Do not need to coordinate actuation of device with inhalation
  o Decrease oropharyngeal deposition, decrease risk of thrush
  o As effective as nebulizer for delivering SABAs and anticholinergics

• Con: bulky

• Products:
  o Available with and without mask
  o Aerochamber, Optichamber, Prochamber, Vortex, etc

• Clean weekly
  o Do not put it in the dishwasher
  o Disassemble
  o Soak in warm water and liquid dish detergent (15 mins)
  o Move pieces around gently in water (1 to 2 mins)
  o Some brands are top rack dishwasher safe
  o Rinse, shake off excess water, and lay out to dry
  o Reassemble
MDI with VHC Technique

- Prime inhaler (if needed)
- Remove cap from inhaler and spacer
- Insert inhaler into spacer and shake well
- Put mouthpiece of spacer into mouth and close lips around it to make a good seal or place mask over mouth and nose
- Stand or sit up straight and breath out completely
- Press down on inhaler one time
- No mask: Inhale slowly and deeply then hold breath for as long as you can (up to 10 seconds)
- Mask: Breath normally for 5 to 6 breaths
- Repeat doing one puff at a time, waiting 15 to 30 seconds between puffs
RespiClick Technique

• Does not need primed or shaken, cannot be used with VHC
• Hold upright with mouthpiece down and uncap, pull cap back until it clicks (this loads a dose)
• Fully exhale away from the inhaler
• Put mouthpiece in your mouth and close lips around it without blocking vent above mouthpiece
• Breath in quickly and deeply
• Remove inhaler from mouth and hold breath for 10 seconds, or as long as you can
• Recap
• If more than one dose is needed, uncap inhaler and repeat steps
• Wipe mouthpiece with a dry tissue, do not use water
SABA Nebulization Solution

- **Albuterol**
  - Individual dose package: 0.63 mg/3 ml, 1.25 mg/3 ml, 2.5 mg/3 ml, 2.5 mg/0.5 ml
  - Multi-dose package: 2.5 mg/0.5 ml (20 ml vial)

- **Levalbuterol**
  - Individual dose package: 0.31 mg/3 ml, 0.63 mg/3 ml, 1.25 mg/3 ml, 1.25 mg/0.5 ml
Nebulizer Technique

• Place the compressor on a flat surface and plug it in
• Wash hands
• Put medication into the nebulizer cup
• Attach tubing to the medication cup and the other end to the air compressor
• Can be used with mouthpiece or mask, generally use a mask for younger children
• Hold mouthpiece in mouth and put lips around it OR put mask on patient making a seal around nose and mouth
• ‘Blow by’ not appropriate
• Flip switch to turn on compressor
• Gently breath in and out while medication mists until there is hardly any or no more mist
• Flip switch to turn off compressor
Ipratropium bromide

- **Use:** Relief of bronchospasm, use in initial hospital management of moderate to severe exacerbations
- **MOA:** bronchodilation through inhibition of cholinergic receptors; may decrease mucous secretion
- **Onset:** 15 minutes
- **Dose**
  - **Inhaler:** 1 to 2 puffs every 6 to 8 hours
    - Acute exacerbation: 4 to 8 puffs every 20 mins as needed for up to 3 hours
  - **Nebulization:** 250 to 500 mcg every 6 hours
    - Acute exacerbation: 250 to 500 mcg every 20 mins x 3 doses
- **Products:**
  - **Inhaler:** 200 puffs/ inhaler; 17 mcg/ inhalation
  - **Nebulization solution:** 0.02% (500 mcg/2.5 ml)
- **ADR:** dry mouth, drying of respiratory secretions, blurred vision if sprayed in eyes
Ipratropium bromide

Technique

• Inhaler
  o Prime before first use of inhaler and if not used for more than 3 days with 2 sprays
  o MDI technique with minor changes
    • No shaking
    • Close eyes so that no medication can be sprayed in eyes

• Nebulization solution
  o Nebulizer technique
Long-term control medications

- Corticosteroids
  - Inhaled Corticosteroids (ICS)
  - Oral Corticosteroids
- Long acting beta agonists (LABA) in combo with ICS
  - Salmeterol
  - Formoterol
  - Vilanterol
- Anticholinergics
  - Tiotropium bromide
- Leukotriene receptor antagonists (LTRA)
  - Montelukast
- Biologics
  - Omalizumab
  - Mepolizumab
  - Benralizumab
  - Dupilumab
  - Reslizumab
Corticosteroids

• MOA
  o Anti-inflammatory
  o Reverse beta_2 receptor downregulation

• Route
  o Inhaled for long term control
    • Higher concentrations delivered directly to the lungs
    • Less systemic exposure, less systemic side effects
  o IV, IM, PO to treat exacerbations
Inhaled Corticosteroids (ICS)

• Use: Long term control of asthma symptoms
• Most consistently effective long-term control medication
  o Reduces symptoms
  o Improves asthma control
  o Prevents exacerbations, reduces number of systemic corticosteroid courses needed
  o Less systemic exposure with ICS then oral or IV steroid doses, less systemic side effects
Side Effects

- Cough, dysphonia, oral candidiasis (thrush); possible systemic effects at high doses (studies not conclusive and clinical significance not established)

- Reduce potential for side effects
  - Use lowest effective dose
    - Evaluate technique
    - Consider adding LABA vs increasing dose of ICS
  - Rinse and spit after inhalation
  - Monitor linear growth of children
  - Review age appropriate dietary intake of calcium and exercise
ICS Inhalers

- Beclomethasone dipropionate (QVAR Redihaler)
- Budesonide (Pulmicort Flexhaler)
- Fluticasone propionate (Flovent HFA, Flovent Diskus)
- Fluticasone furoate (Arnuity Ellipta)
- Mometasone furoate (Asmanex HFA, Asmanex Twisthaler)
- Ciclesonide (Alvesco HFA)
Beclomethasone dipropionate
QVAR RediHaler

• Breath actuated MDI
  o Pro: no need to coordinate inhalation and actuation
  o Con: cannot use with spacer

• Product info
  o 40 mcg/actuation, 80 mcg/actuation
  o 120 doses per inhaler

• Dose: 40 to 160 mcg twice a day
  o Based on disease severity and prior treatment
  o Approved for patients 4 years and older
Breath actuated MDI Technique

- No shaking or actuation
- Open cap and breath out fully
- Place in mouth and make a good seal with lips
- Make sure you do not block air flow on top of inhaler
- Inhale deeply then remove inhaler while holding breath for 5 to 10 seconds
- Close cap (if dose is more than one inhalation must close cap in between puffs)
- Rinse mouth with water and spit it out (ICS)
- Wipe mouthpiece with clean dry cloth, do not put in water
Budesonide

• Inhalation powder: Pulmicort flexhaler
  o Products:
    • 90 mcg/actuation, 180 mcg/actuation
    • Dose: 180 mcg to 360 mcg twice a day
      o Based on disease severity and prior treatment
      o Approved for patients 6 years and older

• Nebulization solution
  o Dose: 0.25 mg to 0.5 mg once or twice daily
  o May be used for patients as young as 6 months
Pulmicort Flexhaler Technique

• Prime if inhaler is new
  o Remove cap and hold upright with one hand gripping the middle of the inhaler
  o Use the other hand to hold the brown grip at the bottom of the inhaler
  o Twist one way as far as it will go then back the other way until it stops

• To take a dose
  o Remove cap and hold upright with one hand gripping the middle of the inhaler
  o Use the other hand to hold the brown grip at the bottom of the inhaler
  o Twist one way as far as it will go then back the other way until it stops (load medication)
  o Exhale completely (away from the inhaler)
  o Place the mouthpiece in your mouth and make a seal around it with your lips
  o Breath in rapidly and deeply
  o Take the inhaler out of your mouth and exhale
  o Rinse mouth with water and spit it out

• Wipe mouthpiece with a dry tissue weekly, do not use water
Fluticasone
Fluticasone propionate inhalation aerosol

- Flovent HFA
  - 44 mcg/actuation, 110 mcg/actuation, 220 mcg/actuation
  - 120 doses per inhaler
  - Dose: 88 mcg to 440 mcg twice a day
    - Based on disease severity and prior treatment
    - Approved for patients 4 years and older
  - MDI technique
    - Rinse mouth with water and spit it out after dose
    - Once weekly clean the inhaler
      - Cotton swab dampened with water to clean the small opening where the medicine sprays out
      - Tissue dampened with water to clean the inside of the mouthpiece
      - Let it air dry overnight then recap
Fluticasone propionate inhalation powder

- Flovent diskus
  - 50 mcg/actuation, 100 mcg/actuation, 250 mcg/actuation
  - 60 doses per inhaler
  - Dose: 50 mcg to 500 mcg twice a day
    - Based on disease severity and prior treatment
    - Approved for patients 4 years and older
  - Diskus inhaler technique
Diskus dry powder inhaler Technique

- Hold diskus level/flat
- Place thumb on thumb grip and push away from you until it clicks, this reveals lever and mouthpiece
- Push lever away from you until it clicks (loads medication)
- Keep diskus level and exhale away from diskus
- Make a seal around the mouthpiece with your lips and inhale rapidly and deeply, over 1 to 2 seconds
- Remove diskus and hold breath for up to 10 seconds, or as long as you can
- Breath out slowly as long as you can
- If a second dose is prescribed, repeat steps, starting with pushing the lever to release another dose
- Use thumb grip to rotate diskus closed, you should hear a click
- Rinse mouth with water and spit it out
- Wipe mouthpiece with a clean cloth weekly and keep closed when not in use
Fluticasone furoate

• Arnuity Ellipta:
  o 50 mcg/actuation, 100 mcg/actuation, 200 mcg/actuation
  o 30 doses per inhaler
  o Inhalation powder

• Dose: 50 mcg to 200 mcg once a day
  o Based on disease severity and prior treatment

• Fluticasone furoate (Arnuity) vs fluticasone propionate (Flovent)
  o FF has a higher binding affinity for the glucocorticoid receptor (1.7 times that of FP)
  o Lower dose of FF vs FP
  o Clinical relevance unknown
Ellipta Technique

• To take a dose
  o Slide cover down until it clicks (loads a dose and decreases dose counter)
  o Exhale fully, away from the inhaler
  o Close your lips around the mouthpiece while not blocking the air vent with your fingers
  o Take one long steady breath
  o Remove inhaler from your mouth and hold your breath for 3 to 4 seconds or as long as you can
  o Breath out slowly and gently
  o Rinse your mouth with water and spit it out
Mometasone furoate

• Asmanex HFA
  o 100 mcg/actuation, 200 mcg/actuation
  o 120 doses per inhaler
  o Dose: 200 mcg to 400 mcg twice a day
    • Based on disease severity and prior treatment
    • Approved for patients 12 and over
  o MDI technique
    • Prime before first use and if not used for more than 5 days (4 sprays)
    • Rinse mouth with water and spit it out after dose
    • To clean, wipe the mouthpiece with a dry tissue at least weekly, do not use water
Mometasone furoate

• Amnanex Twisthaler
  o 110 mcg/actuation; 30 doses per inhaler
  o 220 mcg/actuation; 30, 60, 120 doses per inhaler
  o Dose: 110 mcg once daily to 440 mcg twice daily
    • Based on disease severity and prior treatment
    • Approved for patients 4 years and older
  o Twisthaler technique
Twisthaler Technique

• While holding base, twist white cap counterclockwise to remove, this loads a dose of medication and decreases dose counter
• The arrow should line up with the dose counter
• Exhale away from the inhaler
• Make a seal around the mouthpiece with your lips with the inhaler in a horizontal position making sure not to cover the vent holes
• Breath in quickly and deeply
• Remove inhaler and hold your breath for 10 seconds
• Twist cap back on clockwise (you will hear a click)
• Repeat for second puff if needed
• Wipe mouthpiece with a dry tissue weekly, do not use water
Ciclesonide

- **Alvesco**
  - Inhalation aerosol
  - 80 mcg/actuation, 160 mcg/actuation
  - 60 doses per inhaler
  - Dose: 80 mcg to 320 mcg twice a day
    - Based on disease severity and prior treatment
    - Approved for patients 12 and over
  - MDI technique
    - Prime before first use or not used for 10 days (3 sprays)
    - Rinse mouth with water and spit out after dose
    - Clean mouthpiece weekly with a dry tissue, do not use water
Systemic corticosteroids

• Use to treat exacerbations (“burst”)
  o Prevent progression of exacerbation
  o Reverse inflammation
  o Decrease time to recovery
  o Reduce rate of relapse

• Chronic administration should be reserved for the most severe, difficult to control asthma

• Multiple courses, especially more than three courses in a year is a sign of uncontrolled asthma
Systemic Corticosteroids

• Prednisone/prednisolone (PO)
  o Dose: loading dose: 2 mg/kg (max 60 mg) once, followed by 2 mg/kg daily (max 60 mg) for 4 more days (given once daily or divided into twice daily dosing)
  o Products:
    • Prednisone solution
    • Prednisone tablet
    • Prednisolone base solution
    • Prednisolone sodium phosphate solution (generic Orapred)
    • Prednisolone ODT
  o Patient unable to swallow tablets: prednisolone sodium phosphate solution; better taste than prednisolone base or prednisone
  o Patients are able to swallow tablets: prednisone tablets
  o Inexpensive and typically covered by insurance plans

• Methylprednisolone (IV)
  o Dose: loading dose of 2 mg/kg, followed by 1 mg/kg/dose every 6 hours
  o Typically used for status asthmaticus PICU admission
Systemic Corticosteroids

• Dexamethasone (IV, IM, PO)
  o Dose: 0.6 mg/kg/dose (max 16 mg); 2 doses given 24 to 48 hours apart
  o Products: tablets, solution (0.1 mg/ml; 1 mg/ml), injection (4 mg/ml; 10 mg/ml)
  o At least as effective as 3 to 5 days of prednisone/prednisolone
  o Potential for greater adherence with less doses needed
  o Some studies showed less vomiting than with prednisone/prednisolone
  o Insurance usually does not cover injectable product
    • Caresource may be an exception
# Side effects

**Short term**
- Hyperglycemia
- Increased appetite
- Fluid retention
- Weight gain
- Mood alteration
- Hypertension
- Peptic ulcer

**Long term**
- Adrenal axis suppression
- Growth suppression
- Decreased bone density
- Dermal thinning
- Hypertension
- Diabetes
- Cushing’s syndrome
- Cataracts
- Muscle weakness
- Impaired immune function
Side effects

- Linear growth
  - Delayed by
    - poor control of asthma
    - use of corticosteroids
  - Effect is small with low and medium dose ICS
  - More likely with high dose ICS (but less than oral steroids)
  - Monitor growth
  - Benefit vs risk (potential risks are well balanced by benefits)
Long-acting beta$_2$ agonists (LABA)

- **Use:** long-term control of asthma symptoms
- **MOA:** bronchodilation; stimulates beta2 receptors which leads to relaxation airway smooth muscles through increase in cyclic AMP
- Lipophilic so retained in lung tissue longer than SABA
- Used as adjunctive therapy with ICS
- Not used as monotherapy for long term control
LABA

• Salmeterol
  o Partial beta agonist
  o Onset: 15 mins
  o Duration: at least 12 hours

• Formoterol
  o Full beta agonist
  o More rapid onset of bronchodilation (similar to albuterol)
  o Onset: 5 mins
  o Duration: at least 12 hours

• Vilanterol
LABA safety

• Black box warning
  o Increase in asthma related deaths (salmeterol study)
  o Increase in number of severe asthma exacerbations (formoterol trial in higher dose arm, 48 mcg daily)

• Hypothesis for LABA increase of severe life-threatening exacerbations
  o LABA effects the smooth muscle to cause more severe obstruction when bronchoconstriction occurs
  o Inflammation worsens while LABA maintains lung function leading to more severe obstruction when it does occur or patients may delay seeking treatment until more severe
LABA safety

• Must weigh benefit of LABA for many patients with uncontrolled asthma on ICS alone vs increased risk for severe exacerbation (risk is low but serious)
• For patients not controlled on low dose ICS consider increasing ICS dose or adding LABA, given equal weight in guidelines
• Daily max: 100 mcg salmeterol, 24 mcg formoterol
Corticosteroid/ Long acting beta agonist combination

- Fluticasone propionate/ salmeterol (Advair HFA, Advair Diskus, Wixela Inhub, AirDuo RespiClick)
- Fluticasone furoate/ vilanterol (Breo Ellipta)
- Mometasone furoate/ formoterol (Dulera)
- Budesonide/ formoterol (Symbicort)
Fluticasone propionate/salmeterol

• Advair HFA
  o Inhalation aerosol
  o Available strengths: 45/21, 115/21, 230/21
  o 60 or 120 doses per inhaler
  o Dose: 2 inhalations twice daily
    • Approved for patients 12 years and older
  o MDI technique
    • Prime before first time use (4 sprays) and if not used for more than 4 weeks or dropped (2 sprays)
    • Rinse mouth with water and spit it out after dose
    • Once weekly clean the inhaler
      o cotton swab dampened with water to clean the small opening where the medicine sprays out
      o Tissue dampened with water to clean the inside of the mouthpiece
      o Let it air dry overnight then recap
Fluticasone propionate/salmeterol

- Advair Diskus
  - Dry powder
  - Available strengths: 100/50, 250/50, 500/50
  - 60 doses per inhaler
  - Dose: 1 inhalation twice daily
    - Approved for patients 4 years and older
  - Diskus technique
  - Generic available (Wixela Inhub)
    - Diskus technique
      - Do NOT hold level/flat, instead hold upright with mouthpiece cover down
Fluticasone propionate/salmeterol

• AirDuo Respliclick
  o Dry powder
  o Available strengths: 55/14, 113/14, 232/14 (60 doses per inhaler)
  o Dose: 1 inhalation twice daily
    • Approved for patients 12 years and older
  o RespClick Technique
    • Rinse mouth with water and spit after dose

<table>
<thead>
<tr>
<th></th>
<th>AirDuo RespClick</th>
<th>Authorized Generic</th>
<th>ADVAIR DISKUS®</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fluticasone propionate + Salmeterol</td>
<td>Fluticasone propionate + Salmeterol</td>
<td>Fluticasone propionate + Salmeterol</td>
</tr>
<tr>
<td>Low</td>
<td>55 mcg + 14 mcg</td>
<td>55 mcg + 14 mcg</td>
<td>100 mcg + 50 mcg</td>
</tr>
<tr>
<td>Medium</td>
<td>113 mcg + 14 mcg</td>
<td>113 mcg + 14 mcg</td>
<td>250 mcg + 50 mcg</td>
</tr>
<tr>
<td>High</td>
<td>232 mcg + 14 mcg</td>
<td>232 mcg + 14 mcg</td>
<td>500 mcg + 50 mcg</td>
</tr>
</tbody>
</table>
Fluticasone furoate/vilanterol

- Breo Ellipta
  - Inhalation powder
  - Available strengths: 100/25, 200/25
  - 30 doses per inhaler
  - Dose: 1 inhalation once daily
    - Approved for patients 18 years and older
  - Ellipta technique
Mometasone furoate/formoterol fumarate

• Dulera
  o Inhalation aerosol
  o Available strengths: 100/5, 200/5
  o 120 doses per inhaler
  o Dose: 2 inhalations twice daily
    • Approved for patients 12 years and older
  o MDI technique
    • Prime with before first use and if not used for 5 days (4 sprays)
    • Rinse mouth with water and spit it out after dose
Budesonide/ formoterol fumarate

• Symbicort
  o Inhalation aerosol
  o Available strengths: 80/4.5, 160/4.5
  o Dose: 2 inhalations twice daily
    • Approved for patients 6 years and older
  o 120 inhalations per inhaler
  o MDI technique
    • Prime before first use, if not used for more than 7 days, if dropped (2 sprays)
    • Rinse mouth with water and spit out after dose
    • Wipe mouthpiece with a dry tissue every 7 days
Tiotropium bromide

- **Use:** long term control medication for asthma patients 6 and older
- **MOA:** bronchodilation, long-acting muscarinic antagonist (LAMA)

**Spiriva Respimat**
- Slow moving mist
- 1.25 mcg/ inhalation
- Dose: 2 puffs once daily
- Approved for patients 6 years and older
- Onset: max benefit may take 4 to 8 weeks

- **ADR:** dry mouth, pharyngitis, upper respiratory tract infection
Respimat Inhaler Technique

• When inhaler is new
  o Load cartridge
    • Remove clear plastic cover on base and write in discard date on line provided (3 months)
    • Place narrow end of cartridge into inhaler and push into inhaler, use a hard surface to push cartridge into inhaler, about 1/8 inch will remain outside the inhaler
    • Replace clear plastic cover, you should hear a click when it is in place
  o Prime inhaler
    • Rotate clear plastic base ½ turn in the direction of the arrows until it clicks
    • Open cap, point inhaler at ground, press dose release button, close cap (repeat these steps until you see mist exit the inhaler, then repeat three more times)

• Take a dose
  o Rotate clear plastic base ½ turn in the direction of the arrows until it clicks
  o Open cap and breath out fully
  o Put mouthpiece in mouth while making seal with lips, do not cover airvent on sides
  o Press dose release button while taking a slow, deep breath
  o Remove inhaler from mouth and hold breath for 10 seconds
  o Close cap
  o Repeat for each puff
Montelukast

• Brand name: Singulair
• MOA:
  o Leukotriene receptor antagonist; activation of the receptor is correlated with airway edema, smooth muscle contraction, inflammation
• Can be used as adjunctive therapy with ICS
• Dose:
  o 12 months to 5 years: 4 mg once daily in the evening
  o 6 to 14 years: 5 mg once daily in the evening
  o 15 years and older: 10 mg once daily in the evening
• Dosage forms (generic available)
  o Granules: 4 mg
  o Chewable tablet: 4 mg, 5 mg
  o Tablet: 10 mg
Biologics

• Omalizumab (Xolair)
  o Prevents IgE binding to mast cells and basophils, decreasing release of mediators in allergic response
  o Long-term use decreases exacerbations and steroid use
  o Approved for patients 6 years and older
  o Given subcutaneously every 2 to 4 weeks

• Mepolizumab (Nucala)
  o IL-5 antagonist; reduces production and survival of eosinophils
  o Approved for patients 12 years and older
  o Given subcutaneously every 4 weeks

• Benralizumab (Fasenra)
  o IL-5 antagonist; reduces production and survival of eosinophils
  o Approved for patients 12 years and older
  o Given subcutaneously every 4 weeks

• Reslizumab (Cinqair)
  o IL-5 antagonist; reduces production and survival of eosinophils
  o Approved for patients 18 years and older
  o Given IV every 4 weeks

• Dupilumab (Dupixent)
  o Inhibits IL-4 and IL-13 which are involved in the inflammatory response
  o Approved for patients 12 and older
  o Given subcutaneously every 2 weeks
Referral

• Consider referral to an asthma specialist if patient meets any of the following criteria
  o Difficulty achieving or maintaining asthma control
  o More than 2 steroid bursts in a year
  o Exacerbation requiring hospitalization
  o Step 4 or higher (5 and older)
  o Step 3 or higher (0 to 4 years)
  o Immunotherapy needed
Asthma action plan

**Child Asthma Action Plan**  
*0 to 5 years of age*

<table>
<thead>
<tr>
<th>Long-term control medicines</th>
<th>How much to take</th>
<th>How often</th>
<th>Other instructions (such as spacers/masks, nebulizers)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>times per day</td>
<td>EVERY DAY!</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Quick-relief medicines</th>
<th>How much to take</th>
<th>How often</th>
<th>Other instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Child is well** and has no asthma symptoms, even during active play.

**PREVENT** asthma symptoms every day:
- Give the above long-term control medicines every day.
- Avoid things that make the child’s asthma worse.
  - Avoid tobacco smoke; ask people to smoke outside.

**Child is not well** and has asthma symptoms that may include:
- Coughing
- Wheezing
- Runny nose or other cold symptoms
- Breathing harder or faster
- Awakening due to coughing or difficulty breathing
- Playing less than usual

Other symptoms that could indicate that your child is having trouble breathing may include: difficulty feeding (grunting sounds, poor sucking), changes in sleep patterns, cranky and tired, decreased appetite.

**Child feels awful!** Warning signs may include:
- Child’s wheeze, cough, or difficulty breathing continues or worsens, even after giving Yellow Zone medicines.
- Child’s breathing is so hard that he/she is having trouble walking/talking/eating/playing.
- Child’s skin is so hard and dry it makes it difficult to feel for a pulse.
- Child’s skin is so hard that he/she is having trouble walking/talking/eating/playing.
- Child is droopy or less alert than normal.

**Call 9-1-1 if:**
- Child’s skin is sucked in around neck and ribs, or
- Lips and/or fingernails are gray or blue, or
- Child does not respond to you.

**CAUTION.** Take action by continuing to give regular asthma medicines every day and:
- Give
  - (Include dose and frequency)

If the child is not in the Green Zone and still has symptoms after one hour then:
- Give more
  - (Include dose and frequency)

**MEDICAL ALERT!** Get help!
- Take the child to the hospital or call 9-1-1 immediately!
- Give more
  - until you get help. (Include dose and frequency)
- Give
  - (Include dose and frequency)

**NOTE:** If this medicine is needed often (________ times per week), call clinician.

**Dayton Children’s**