Disclosures

• Betsy, Zach, and Steve work for Rocky Mountain Health Plans.
• We do not have any financial interest in the medications we are discussing today.
• We have no intention to malign any person, business or product.
Question 1

• Which best describes you...
  – A) Physician
  – B) Pharmacist
  – C) Physician Assistant/Nurse Practitioner
  – D) Nurse
  – E) Other
  – F) I’m indescribable
Question 2

• Choose...
  – A) I have attended many PharmSuitables before
  – B) I have attended 1 or 2 PharmaSuitables before
  – C) This is my first time attending PharmSuitables
  – D) I’m not sure what I’m attending
Question 3

• I have been practicing...
  – A) less than 3 years
  – B) 3-10 years
  – C) 11-20 years
  – D) 21+ years
  – E) I’m older than dirt
Question 4

- Prescriber Specialty
  - A) Family Practice
  - B) Internal Medicine
  - C) Pediatrician
  - D) Other prescriber specialty
  - E) Not a prescriber
Naloxone...

• Effective June 1, the following have ZERO copay for all RMHP membership
  – Narcan® Nasal Spray
  – Naloxone 0.4mg/mL vial (kit with syringe)
  – Naloxone prefilled syringe 1mg/mL (kit with syringe, cartridge) –
    • to be used with atomizer (obtained separately) for nasal administration
Naloxone...

• Competitive antagonist of the mu opioid receptor, temporarily displaces and reverses opioid effects
• High first pass effect, not suitable for oral administration
• Duration of effect, 30-60min
• Short onset of action, averages 2 (IV) – 5 (IM/Nasal) minutes
• No effect in the absence of opioids
Naloxone...

- NOT covered
  - Evzio® talking autoinjector
  - This slick device is preloaded with naloxone and talks you through the administration
  - Why isn’t it covered?
Why isn’t Evzio talking injector covered by insurance?

• A) because it is less effective than other forms of naloxone, including intranasal
• B) because it costs almost $4,000 for a twin pack
• C) because it costs almost $400 for a twin pack
• D) because it’s more expensive AND less effective
• E) because it isn’t FDA approved
Clip that coupon

<table>
<thead>
<tr>
<th>Price Effective Date</th>
<th>Unit</th>
<th>Pkg Size</th>
<th>Price / Pkg Size</th>
<th>Pkg Qty</th>
<th>Price / Pkg Qty</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-12-2016</td>
<td>$6,150.00/ML</td>
<td>0.4 ML</td>
<td>$2,460.00/Package</td>
<td>2 Package</td>
<td>$4,920.00</td>
</tr>
</tbody>
</table>

Walgreens  Evzio 1 carton (2 auto-injectors) 0.4mg

- Prices
- Nearby Locations

**Coupon Price**  $3,980.00

1. Get the coupon using the button on the right.
2. Present the coupon to your pharmacist.
3. Pay the coupon price of $3,980.00
Narcan® Nasal Spray

Prefilled with 4mg of naloxone in a 0.1 mL spray device, ready to go

Package of two devices, ~$130

Do NOT prime or test the device
Naloxone/atomizer for nasal administration

Requires separate purchase of prefilled cartridge and nasal atomizer device, total cost ~ $60
Naloxone/atomizer for nasal administration

Dose half syringe contents into each nostril. Total dose is 2mg (vs. 4mg for Narcan®)
Naloxone/atomizer for nasal administration

Shelf life 12-18 months

Two weeks once assembled
Naloxone for injection

Least costly option
(about $30)
Requires correctly inserting the syringe needle into the vial, extracting the contents, and injecting the drug
Herpes Zoster

• The new vaccine for preventing Shingles is...
  • A) Zostavax
  • B) Rid-Shingle
  • C) Shingrix
  • D) Zosterzap
  • E) None of these
Shingrix for Shingles

• Second vaccine approved by FDA for prevention of herpes zoster
• Non-live, recombinant vaccine
  – Zostavax is live, attenuated vaccine
Shingrix for Shingles

• Zostavax quick facts
  – Initial efficacy ages 50-59 is about 70%
  – Efficacy ages 60-69 is 64%, ages 70-79 is 41%
  – Low efficacy in older adults (~18% in 80 year olds)
  – Efficacy quickly diminished over time (as low as 19% in a 7 year study)
  – Contraindicated in immunocompromised
  – Given as single injection
  – Cost, AWP $267
Shingrix for Shingles

• Shingrix quick facts
  – High initial efficacy
    • ~97% effective for ages 50-69 (n=11,324)
      – 5 cases vs. 162 on placebo
    • 91% effective ages 70-79 (n=13,022)
      – 19 cases vs. 216 on placebo
    • 91% effective in ages over 80 (n=3,574)
      – 6 cases vs. 68 on placebo
    • Overall efficacy age over 50 years is 91.2% (n=27,920)
  – Appears to maintain efficacy over time
    • 88% to 93% four years post-vaccination
# Shingrix for Shingles

## Vaccine Efficacy Against Overall PHN

<table>
<thead>
<tr>
<th>Cases of PHN in the clinical trials†</th>
<th>SHINGRIX</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGES 50–69*</td>
<td>0/5631</td>
<td>10/5689</td>
</tr>
<tr>
<td>AGES ≥70</td>
<td>4/8250</td>
<td>36/8346</td>
</tr>
</tbody>
</table>

### SHINGRIX efficacy against PHN†

| AGES 50†                            | 91.2%     | (75.9, 97.7) |
| AGES ≥70†                           | 88.8%     | (68.7, 97.1) |
Shingrix for Shingles

• Shingrix quick facts
  – Higher rates of injection site pain than Zostavax
    • Pain 79% vs. 35-55%, erythema & swelling similar
  – Not contraindicated in immunocompromised
  – Given as two **IM** injections 2 – 6 months apart
    (Zostavax is one **SC** inj)
  – ACIP recommends over Zostavax, ≥50 years
  – Cost, AWP $168 per injection
    ($336 for series)
Zostavax fights back

This might be hard to say...

“Single-shot shingles shot”

...but starting a conversation about ZOSTAVAX can be easy.
Shingrix for Shingles

- VAERS (vaccine adverse event reporting system) – part of CDC
  - Began monitoring Shingrix on 10/2017
  - Over 4 months, looked at 155 reports about Shingrix
    - 13 were at least 1 error in administration of the vaccine
    - 9 errors were SC rather than IM injection
      - 8 of 9 caused pain, redness, itching at injection site
    - One SC recipient was 48 years old
    - Two got Zostavax literature rather than Shingrix
    - One patient was 39 y.o.
    - 1 case was incorrect storage (must refrigerate, discard reconstituted w/in 6 hours)
    - 1 case was incorrect reconstitution (received only part of the vaccine, no antigen)
Clicker Question

• How many times during your career have you thought “I wish I had a blood pressure drug and an NSAID in a combination pill”?
  A) Never
  B) Every so often
  C) I can think of a few patients that would benefit from it
  D) This will be a game changer. I will switch all my patients to this combo
Consensi

• Combination drug
  – Amlodipine besylate
  – Celecoxib

• Indication
  – For patients for whom treatment with amlodipine for hypertension and celecoxib for osteoarthritis are appropriate

• Limitation of use
  – Celecoxib only available as 200mg dose and is only taken once daily
Consensi

• Dosing
  – Initiate at 2.5mg amlodipine/200mg celecoxib and titrate every 7-14 days
  – Maximum dosing 10mg/200mg per day

• Black box warnings and adverse effects are based on individual components
  – Abdominal pain, diarrhea, dyspepsia, flatulence, peripheral edema, accidental injury, dizziness, pharyngitis, rhinitis, sinusitis, upper respiratory tract infection, rash.
Consensi Phase III Trial Design
(under Special Protocol Assessment from FDA)

Newly diagnosed Hypertensive patients

Double-blind, placebo-controlled, multi-center study

\[ N = 152 \]

4-arm trial with 30-45 patients in each arm

2 weeks of treatment

Consensi: Celecoxib 200 mg + Amlodipine 10 mg

AMLODIPINE 10 mg

CELECOXIB 200 mg

PLACEBO

Data Collection and Statistical Analysis

Primary endpoint
Demonstrate that the reduction in blood pressure in the ConsensiTM arm is at least 50% of the reduction in the amlodipine arm

Measurement of pain was not required by FDA
**Consensi Phase III Trial Results**

- Primary efficacy endpoint was successfully achieved (P=0.001)
- Demonstrated 2.5x better blood pressure reduction than FDA requirement (50% of amlodipine arm)
- Demonstrated consistent reduction in all measures of blood pressure
- Observed beneficial renal functions:

<table>
<thead>
<tr>
<th>Measure</th>
<th>Consensi</th>
<th>Amlodipine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine plasma level reduction</td>
<td>-3.22 mol/L</td>
<td>-2.55 mol/L</td>
</tr>
<tr>
<td>Peripheral edema (% patients)</td>
<td>8.2%</td>
<td>15.6%</td>
</tr>
</tbody>
</table>

**Blood Pressure Reduction of Consensi vs. Amlodipine and Celecoxib**

- Consensi demonstrated even better BP reduction than same amount of amlodipine given without celecoxib

**Error bars – standard error of mean**

- Additional Phase III/IV clinical trial to scientifically validate the renal benefits (not required for NDA submission) was completed. Topline results were announced in October, 2017
• Consensi US Target Markets

• Consensi™ targets osteoarthritic patients currently treated with NSAIDs
• (celecoxib as well as others) who also suffer from existing or newly diagnosed hypertension

Lonhala Magnair is the first glycopyrrolate formulation approved for treatment of COPD
A) True
B) False
Lonhala Magnair

• The first nebulized Long-acting muscarinic antagonist
• Glycopyrrolate inhalation solution
• There are four hand-held LAMA inhalers currently on the market:
  – Spiriva Handihaler/Respimat (tiotropium)
  – Seebri Neohaler (glycopyrrolate)
  – Incruse Ellipta (umeclidinium)
  – Tudorza Pressair (aclindinium)
Lonhala Magnair

• Indication
  – Long-term, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD)

• Dosing
  – Inhale contents of one vial (25 mcg) twice-daily using Magnair inhaler

• Adverse effects:
  – Dyspnea (4.9% with Lonhala vs 3.0 with placebo)
  – Urinary tract infection (2.1% vs. 1.4%)
Lonhala Magnair

• Advantages
  – Nebulized solution offering a unique delivery of a long-acting muscarinic antagonist
  – No hand-breath coordination required

• Disadvantages
  – Glycopyrrolate is available in other formulations
  – Does not offer improved efficacy or safety over other formulations (improves FEV₁ by about 0.1 L over placebo)
  – Device must be assembled
Lonhala Magnair

<table>
<thead>
<tr>
<th></th>
<th>Lonhala Magnair</th>
<th>Seebri Neohaler</th>
<th>Spiriva Respimat</th>
<th>Incruse Ellipta</th>
<th>Tudorza Pressair</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost (AWP/month)</td>
<td>$1,359</td>
<td>$473</td>
<td>$477</td>
<td>$389</td>
<td>$410</td>
</tr>
<tr>
<td>Dosing</td>
<td>Twice daily</td>
<td>Twice daily</td>
<td>Once daily</td>
<td>Once daily</td>
<td>Twice daily</td>
</tr>
</tbody>
</table>

- **Marketing strategy**
  - Since the nebulizer solution and device were approved together, the device is considered part of the drug
  - Will be a Medicare Part D drug instead of Medicare Part B like other nebulizers
Clicker Question

- This treatment for clostridium difficile-associated diarrhea is most likely to prevent recurrence
  A) metronidazole (Flagyl)
  B) fidaxomicin (Dificid)
  C) IV vancomycin
  D) Fecal Microbiota Transplant (FMT)
  E) Oral vancomycin
FIRVANQ™
(vancomycin hydrochloride) for oral solution

For Oral Use Only
Vancomycin Hydrochloride Powder for Oral Solution Kit
Vancomycin 50 mg/mL in Grape Flavored Diluent

Each Kit Includes:
- 1 sterile, overaseptic vial containing
- 1 sterile, overaseptic vial containing
- 1 bottle containing 380 mL, Grape Flavored Diluent

Each vial contains 50 mg Vancomycin

The only FDA approved
vancomycin hydrochloride for oral solution,
traditional compounding no longer required

Vancomycin 25 HCl mg/mL
powder for oral solution kit
Two sizes & NDC:
150 mL as dispensed: 65628-204-05
300 mL as dispensed: 65628-205-10

Vancomycin 50 HCl mg/mL
powder for oral solution kit
Two sizes & NDC:
150 mL as dispensed: 65628-206-05
300 mL as dispensed: 65628-208-10
Firvanq

- Vancomycin oral solution – Grape flavored
- Replaces First-vancomycin on the market
- Indications:
  - Clostridium difficile-associated diarrhea
  - Enterocolitis caused by Staphylcoccus aureus [including methicillin-resistant strains (MRSA)]
- Approved for adults and pediatric patients less than 18 years of age

**Effective April 2, 2018**
FIRST Kit Vancomycin has been **discontinued**
• Dosing
  – Clostridium difficile:
    • Adults (18+): 125mg PO 4 times per day for 10 days
    • Pediatric (<18): 40mg/kg 3-4 divided doses for 7-10 days with total daily dose not to exceed 2 grams
  – Staphylococcal enterocolitis:
    • Adults (18+): 500mg – 2g PO in 3-4 divided doses for 7-10 days
    • Pediatric (<18): 40mg/kg in 3-4 divided doses for 7 – 10 days not to exceed 2 grams/day
Firvanq

• Adverse Effects:
  – Nausea (17%), abdominal pain (15%) and hypokalemia (13%)

• Special Population:
  – In patients 65+, including those with normal renal function prior to treatment, renal function should be monitored during and following treatment with to detect potential vancomycin induced nephrotoxicity
Firvanq

• Clinical Trials
  – N = 266
  – CDAD defined as ≥3 loose or watery bowel movements w/in 24 hrs preceding enrollment and confirmation of C. difficile toxin A/B or pseudomembranes
  – Efficacy was defined as diarrhea resolution and the absence of severe abdominal discomfort due to CDAD, on day 10.
Firvanq

Table 4: Clinical Success Rates (Full Analysis Set)

<table>
<thead>
<tr>
<th>Trial</th>
<th>Clinical Success Rate Vancomycin Hydrochloride % (N)</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial 1</td>
<td>81.3 (134)</td>
<td>(74.4, 88.3)</td>
</tr>
<tr>
<td>Trial 2</td>
<td>80.8 (125)</td>
<td>(73.5, 88.1)</td>
</tr>
</tbody>
</table>

• Time to resolution of diarrhea
  – Trial 1: 5 days
  – Trial 2: 4 days

• Recurrence rates of CDAD during the following four weeks were:
  – Trial 1: 23%
  – Trial 2: 18%
Firvanq

• Important Administration Instructions
  – Shake the reconstituted solutions of Firvanq well before each use and to use an oral dosing device that measures the appropriate volume of the oral solution in milliliters.
  – Store the reconstituted solutions of Firvanq in the refrigerator when not in use.
  – Discard reconstituted solutions of Firvanq after 14 days, or if it appears hazy or contains particulates
<table>
<thead>
<tr>
<th></th>
<th>Firvanq</th>
<th>Vancomycin capsule</th>
<th>Metronidazole</th>
<th>Dificid</th>
<th>FMT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost (AWP/standard course)</td>
<td>$150</td>
<td>$462</td>
<td>$13</td>
<td>$4,418</td>
<td>$300-$400</td>
</tr>
<tr>
<td>Recurrence rates</td>
<td>25-35%</td>
<td>25-35%</td>
<td>25-35%</td>
<td>15-20%</td>
<td>5-10%</td>
</tr>
</tbody>
</table>
Why is my asthma patient no better?

• 28 yo female with complaints of cough, mild DOE; cough is mostly in the evenings and at night. Using a SABA with minimal relief. She experiences 3-4 nighttime awakenings per week.

• Should you intensify her regimen and label as her as moderate persistent asthma and start an ICS?

• OR dig deeper?

• Do spirometry?
## Classification of Asthma Severity

### Components of Severity

<table>
<thead>
<tr>
<th>Impairment</th>
<th>Intermittent</th>
<th>Persistent</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week but not daily</td>
<td>Throughout the day</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>≤2x/month</td>
<td>3–4x/month</td>
<td>Daily</td>
</tr>
<tr>
<td>Short-acting beta-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>Several times per day</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
<td>Minor limitation</td>
<td>Some limitation</td>
</tr>
<tr>
<td>Normal FEV₁/FVC:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8–19 yr</td>
<td>85%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–39 yr</td>
<td>80%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40–59 yr</td>
<td>75%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60–80 yr</td>
<td>70%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal FEV₁ between exacerbations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV₁ &gt;80% predicted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV₁/FVC normal</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Risk

- Exacerbations requiring oral systemic corticosteroids:
  - 0–1/year (see note)
  - ≥2/year (see note)

**Consider severity and interval since last exacerbation.**

**Frequency and severity may fluctuate over time for patients in any severity category.**

**Relative annual risk of exacerbations may be related to FEV₁.**

### Recommended Step for Initiating Treatment

- **Step 1**
  - In 2–6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.

- **Step 2**
  - Step 3
  - and consider short course of oral systemic corticosteroids

**See “Stepwise Approach for Managing Asthma” for treatment steps.**
<table>
<thead>
<tr>
<th>Components of Control</th>
<th>Classification of Asthma Control (≥12 years of age)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Well Controlled</td>
</tr>
<tr>
<td>Impairment</td>
<td></td>
</tr>
<tr>
<td>Symptoms</td>
<td>≤2 days/week</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>≤2x/month</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
</tr>
<tr>
<td>Short-acting beta₂-agonist use for symptom control (not prevention of EIB)</td>
<td>≤2 days/week</td>
</tr>
<tr>
<td>FEV₁ or peak flow</td>
<td>&gt;80% predicted/personal best</td>
</tr>
<tr>
<td>Validated questionnaires</td>
<td></td>
</tr>
<tr>
<td>ATAQ</td>
<td>0</td>
</tr>
<tr>
<td>ACQ</td>
<td>≤0.75*</td>
</tr>
<tr>
<td>ACT</td>
<td>≥20</td>
</tr>
<tr>
<td>Exacerbations requiring oral systemic corticosteroids</td>
<td>0–1/year</td>
</tr>
<tr>
<td>Risk</td>
<td></td>
</tr>
<tr>
<td>Progressive loss of lung function</td>
<td>Evaluation requires long-term followup care.</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>
</tr>
</tbody>
</table>

**Recommended Action for Treatment**

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

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

- Step up 1 step.
- Reevaluate in 2–6 weeks.
- For side effects, consider alternative treatment options.

- Consider short course of oral systemic corticosteroids.
- Step up 1–2 steps.
- Reevaluate in 2 weeks.
- For side effects, consider alternative treatment options.
**FIGURE 16. STEPWISE APPROACH FOR MANAGING ASTHMA IN YOUTHS ≥12 YEARS OF AGE AND ADULTS**

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

**Step 2**
*Preferred:* Low-dose ICS
*Alternative:* Medium-dose ICS

**Step 3**
*Preferred:* Medium-dose ICS + LABA
*Alternative:* Low-dose ICS + either LTRA, Theophylline, or Zileuton

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

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

**Step 6**
*Step up if needed (first, check adherence, environmental control, and comorbid conditions)*

**Step down if possible (and asthma is well controlled at least 3 months)**

**Key:**
Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy. ICS, inhaled corticosteroid; LABA, long-acting inhaled beta2-agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta2-agonist

**Notes:**
- The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.
- If alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.
- Zileuton is a less desirable alternative due to limited studies as adjunctive therapy and the need to monitor liver function. Theophylline requires monitoring of serum concentration levels.
- In step 6, before oral corticosteroids are introduced, a trial of high-dose ICS + LABA + either LTRA, theophylline, or zileuton may be considered, although this approach has not been studied in clinical trials.
- Step 1, 2, and 3 preferred therapies are based on Evidence A; step 3 alternative therapy is based on Evidence A for LTRA, Evidence B for theophylline, and Evidence D for zileuton. Step 4 preferred therapy is based on Evidence B, and alternative therapy is based on Evidence B for LTRA and theophylline and Evidence D zileuton. Step 5 preferred therapy is based on Evidence B. Step 6 preferred therapy is based on (EPR—2 1997) and Evidence B for omalizumab.
- Immunotherapy for steps 2–4 is based on Evidence B for house-dust mites, animal danders, and pollens; evidence is weak or lacking for molds and cockroaches. Evidence is strongest for immunotherapy with single allergens. The role of allergy in asthma is greater in children than in adults.
- Clinicians who administer immunotherapy or omalizumab should be prepared and equipped to identify and treat anaphylaxis that may occur.
How spirometry can help

- On further questioning, she never had “asthma” until she had kids. Her BMI is 33. She also suffers from reflux. Notes seasonal allergies.
- Spirometry shows FEV1 +90% of predicted with minimal response to bronchodilators
- Consider: treating reflux, allergies, (and BMI) and NOT starting an ICS
- Use spirometry to help; full PFTs unnecessary
Multiple admissions for asthma

• 26 yo male s/p 1 admission and 3 ED visits in the last 6 months for asthma exacerbation.
• Medications include Fluticasone inhaler 110 mcg/ACT, 1 puff twice daily, Albuterol MDI prn.
• Usually responds well to a short course of prednisone.
• Possibilities for trying to decrease asthma exacerbations:
  • 1) more history re exposure, 2) increase baseline ICS dose after exacerbations, 3) make sure he knows how to use his inhalers----kind of basic but very important
## Stepwise Approach for Managing Asthma Long Term in Children, 0–4 Years of Age and 5–11 Years of Age

### Children 0–4 Years of Age

#### Step 1: Intermittent Asthma
- Preferential: SABA PRN
- Alternative: Cromolyn or Montelukast

#### Step 2: Persistent Asthma: Daily Medication
- Preferred: Low-dose ICS
- Optional: LABA, LTRA, or Theophylline

#### Each Step: Patient Education and Environmental Control
- Quick-Relief Medication: SABA as needed for symptoms. With viral respiratory symptoms: SABA 4–6 hours up to 24 hours (longer with physician consult).

#### Step 3: Assess Control
- Step up if needed (first check inhaler technique, adherence, environmental control, and comorbid conditions)

#### Step 4: Step 5: Step 6
- Step down if possible (and asthma is well controlled at least 3 months)

### Notes
- The stepwise approach is meant to assist, not replace, the clinical decision-making required to meet individual patient needs.
- If an alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.
- If clear benefit is not observed within 4–6 weeks, and patient’s family’s medication technique and adherence are satisfactory, consider adjusting therapy or an alternative diagnosis.
- Studies on children 0–4 years of age are limited. Step 2 preferred therapy is based on evidence A. All other recommendations are based on expert opinion and extrapolation from studies in older children.
- Clinicians who administer immunotherapy should be prepared and equipped to identify and treat anaphylaxis that may occur.

### Key:
- Alphabetical listing is used when more than one treatment option is listed within either preferred or alternative therapy. ICS, inhaled corticosteroid; LABA, inhaled long-acting beta₂-agonist; LTRA, leukotriene receptor antagonist; oral corticosteroids, oral systemic corticosteroids; SABA, inhaled short-acting beta₂-agonist

### Children 5–11 Years of Age

#### Step 1: Intermittent Asthma
- Preferential: SABA PRN
- Alternative: Cromolyn, LTRA, Nedocromil, or Theophylline

#### Step 2: Persistent Asthma: Daily Medication
- Preferred: Low-dose ICS
- Optional: LABA, LTRA, or Theophylline
- Alternative: Medium-dose ICS

#### 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.
### Daily doses for inhaled glucocorticoids in children

<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 to 4</td>
<td>Child 5 to 11</td>
<td>Child 0 to 4</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>80 to 160 mcg</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>180 to 400 mcg</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>0.25 to 0.5 mg</td>
<td>0.5 mg</td>
<td>&gt;0.5 to 1.0 mg</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>160 mcg</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>176 mcg</td>
<td>88 to 176 mcg</td>
<td>&gt;176 to 352 mcg</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>100 to 200 mcg</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>110 mcg</td>
<td>NA</td>
</tr>
</tbody>
</table>

Inappropriate dosing is the clinician’s judgment of the patient’s response to therapy. The clinician must monitor the patient’s response on several clinical parameters and adjust the dose of medication based on the minimum dose required to maintain control, thus reducing the potential for age labeling, especially in the high-dose range. Budesonide nebulizer suspension is the only ICS with FDA approved labeling for children <4 years of age. Metered-dose inhaler (MDI) dosenit of the drug leaves the actuator and delivered to the patient), which is the labeling required in the United States. This is different from the dosage expressed as the valve dose (the available to the patient), which is used in many European countries and in some scientific literature. Dry powder inhaler (DPI) doses are expressed as the amount of drug in the inhaler, safety and efficacy of ICSs in children <1 year has not been established. Children <4 years of age generally require delivery of ICS (budesonide and fluticasone HFA) through a face mask getting the medication in the eyes. Wash face after each treatment to prevent local corticosteroid side effects. For budesonide, the dose may be administered one to three times daily, and levosalbuterol nebulizer solutions in the same nebulizer. Use only jet nebulizers, as ultrasonic nebulizers are ineffective for suspensions. For fluticasone HFA, the dose is higher than for children 5 to 11 years of age due to lower dose delivered with face mask and data on efficacy in young children. Not approved and no data available for this age group; DPI: dry powder inhaler; MDI: metered dose inhaler; ICS: inhaled corticosteroid; FDA: US Food and Drug Administration.
SPACERS!!

• You can do away with masks for the spacer once a child knows how to inhale if you tell them to take a big breath in; Masks decrease drug delivery a little.

• Consider having your asthma patient, (or COPD patient) show you how they use their inhaler.

• Ask about the last time they had it refilled—especially the rescue inhaler