Asthma Pharmacology: Medications and Devices

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Objectives

Upon completion of this workshop participants will be able to:

◦ Classify the different medications used to treat asthma

◦ Describe the correct technique for the devices used to deliver those medications

◦ List the correct priming and cleaning instructions for each type of device
Patient education at EVERY encounter
LOOKING AHEAD TO EPR-4

EPR-4 Update in 2018
NHLBI Advisory Council

Asthma Topics

1. Role of Adjustable Medication Dosing in Recurrent Wheezing and Asthma

2. Role of Long Acting Anti-Muscarinic Agents (LAMAs) in Asthma Management as Add-on to ICSs

3. Role of Bronchial Thermoplasty in Adult Severe Asthma

4. Role of Fractional exhaled Nitric Oxide (FeNO) in Diagnosis, Medication Selection, and Monitoring Treatment Response in Asthma

5. Role of Remediation of Indoor Allergens (e.g., House Dust Mites/Animals/Pests) in Asthma Management

6. Role of Immunotherapy in Treatment of Asthma
Stepwise management - pharmacotherapy

**Not for children <12 years**

**For children 6-11 years, the preferred Step 3 treatment is medium dose ICS**

For patients prescribed BDP/formoterol or BUD/formoterol maintenance and reliever therapy

- Tiotropium by mist inhaler is an add-on treatment for patients ≥12 years with a history of exacerbations
- Low-dose fluticasone furoate/vilanterol an option for Step 3

**GINA 2016, Box 3-5 (2/8) (upper part)**
Delivery Devices
Characteristics of Inhaled Particles

- Deposition varies with devices
- Particle size varies by device
- Emulsifiers (stabilizing agent designed to encourage suspension of ingredients)
- Excipients (an inert substance that forms a vehicle for the active drug)
  - Must have no interaction with drug
  - Must be stable for handling
  - Must be pharmacologically inert
Particle Size of ICS

(Buhl Allergy 2006)
Respiratory Tract Deposition

Deposition %

Log aerodynamic diameter μm

Total
Oropharynx
Bronchial/conducting airways
Alveolar

Courtesy R. Pleasants
Characteristics of Pressurized Metered Dose Inhalers (pMDI)

- Propellants
- Drug formulation
- Solution vs. suspension
- Particle size
- Built in spacer (Aerospan)
- [Breath actuated DPI (ProAir Respiclick)]
- Not all have counters
- Number of doses per device varies (handout)
- Priming and Cleaning varies with device (handout)

Newman, S. Principles of Metered-Dose Inhaler Design, Resp Care, Sept 2005, V 50 No 9
Components of a pMDI

- Canister
- Gas phase
- Liquid phase (formulation)
- Retaining cup
- Actuator
- Metering chamber
- Metering valve
- Expansion chamber
- Actuator nozzle
- High-velocity spray
## Choosing an inhaler device for children ≤5 years

<table>
<thead>
<tr>
<th>Age</th>
<th>Preferred device</th>
<th>Alternate device</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–3 years</td>
<td>Pressurized metered dose inhaler plus dedicated spacer with face mask</td>
<td>Nebulizer with face mask</td>
</tr>
<tr>
<td>4–5 years</td>
<td>Pressurized metered dose inhaler plus dedicated spacer with mouthpiece</td>
<td>Pressurized metered dose inhaler plus dedicated spacer with face mask, or nebulizer with mouthpiece or face mask</td>
</tr>
</tbody>
</table>
Characteristics of Dry Powder Inhalers (DPI)

- For use by those 4 years of age and older
- Can NOT be used with a VHC
- Requires rapid (2-3 seconds) deep inhalation followed by a 10-second breath-hold
- Some devices are sensitive to moisture or to damage to the dosing mechanism if dropped
- Number of doses per device varies (handout)
- Priming and Cleaning varies with device (handout)

Components of DPI
Devices Used to Aid Medication Delivery

- Spacers and Valved Holding Chambers (VHC) increase medication delivery to the lower airways
  - By reducing oral deposition of particles and
  - By enhancing activation-inhalation coordination
- Spacer is a generic term for any open tube placed on the pMDI mouthpiece to extend its distance from the mouth
- VHCs are manufactured with a one-way valve that prevents exhalation into the device
- NOT used with breath actuated devices or DPIs
Valved Holding Chambers

• Most MDI’s should be used with a holding chamber or spacer
  ◦ Holding chambers are better because they have valves that keep the medicine inside the chamber until it is inhaled

• MDI’s used alone deposit much of the medication in the mouth, throat or stomach depending on technique
Metered Dose Inhaler Steps

- Remove cap
- Check for foreign body
- Insert inhaler into holding chamber
- *Shake for 5 seconds
- *Stand, tilt head back or keep level
- *Exhale to function residual
- *Place mouthpiece in mouth/mask firmly over face
- *Actuate canister once
- *Take a slow, deep breath and hold for 5+5 seconds
- *For mask, hold mask over face until child takes 5 to 6 breaths
- *Remove mouthpiece/mask and exhale
- Wait 30-60 seconds
- Repeat * steps replacing cap after second puff
- After last puff rinse mouth and spit out water if ICS
- Wipe face with damp cloth if using mask
- Describe how to determine if MDI is empty
Dry Powder Inhaler Steps

- Remove cover
- Check foreign body
- Load dose
- Tilt head back or keep level
- Exhale (away from inhaler) to functional residual
- Place mouthpiece in mouth
- Initiate deep breath
- Hold breath for 10 seconds (5+5)

- Remove from mouth and exhale
- If additional puffs ordered wait 60 seconds and repeat steps
- Loading second dose varies with device
- Replace cover
- After last puff rinse mouth and spit out water if ICS
- Describe how to determine if DPI is empty
Pro Air RespiClick® Inhaler Steps

- Make sure cap is closed before each dose
- Hold inhaler in upright position to open
- Open cap fully (this loads the dose)
- Put mouthpiece in mouth and close lips
- Make sure vent at top of mouthpiece is not obstructed
- Breath in deeply through the mouth

- Hold breath for about 10 seconds, then exhale
- Close the cap
- Repeat steps for second dose
Valved Holding Chambers

- Valved holding chambers (VHC) should be cleaned weekly
  - Wash all parts of your holding chamber in warm soapy water
  - DO NOT rinse off the soapy water, just let the spacer air dry
  - DO NOT share chambers
  - Replace the holding chamber if the valve does not open and close completely
CPT Code for Teaching Inhaler

- **94664**: Demonstration and/or evaluation of patient utilization of an aerosol generator, nebulizer, metered dose inhaler or IPPB device
- Education must be given separate from a nebulizer treatment
Valved Holding Chambers
Flexichamber
Characteristics of Nebulizers

- Allow for drug delivery in individuals who cannot use MDIs or DPIs
- Optimal technique requires slow tidal breathing with occasional deep breaths
- Never use “blow by” (holding the open tube or mask near the individual’s nose or mouth)
- More expensive and time-consuming than MDIs with VHCs, and output dependent on device and operating parameters
- If not cleaned properly, there is a risk for transmission of bacterial infections
- After each use, take apart the nebulizer and wash all parts (except tubing and finger valve) in liquid dish soap and water. Rinse with water and shake off any excess. Reattach the nebulizer pieces and tubing to the air compressor and turn on the compressor to dry the nebulizer quickly. Make sure the nebulizer is completely dry before storing.

Nebulizer Components
One Time Use Nebulizer Cup
Reusable Nebulizer Cups

Pari LCs

Aero-Eclipse

Respironics Sidestream
Pedi-neb Pacifier
Checking Inhaler Technique

- Most patients use devices incorrectly even when given good instructions
- Good technique can become bad between visits
- Most health care providers are not able to demonstrate good technique
- A reliable, validated device does exist to check inhaler technique
In-check Dial

- Device used to check inhaler technique
- Billable teaching
- Should be used at every visit to confirm proper inhaler technique

<table>
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<tr>
<th>Inhaler</th>
<th>L/min 20</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
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<th>90</th>
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<tbody>
<tr>
<td>Accuhaler / Diskus</td>
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<td>Turbuhaler / Turbohaler</td>
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<td>Easi-breathe / Surehaler</td>
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<td>Low resistance pMDI</td>
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Optimum Inspiratory Flow

June 2000
Original In-Check Dial

Scale
(30 - 370 l/min)

Mouthpiece

Magnet & Weight

Pointer (red)

in-check
New In-Check Dial
Asthma Medications
Types of Asthma Medications

- Divided into two categories
  - Controllers - used everyday even when patient does not have symptoms
  - Relievers - taken at first sign of symptoms to prevent worsening
Controllers

- **Inhaled Corticosteroids (ICS)**
  - Anti-inflammatory; works on multiple mediators of asthma to reduce inflammation

- **Nedocromil**-no longer available

- **Cromolyn**-no longer available

- **Leukotriene Receptor Antagonists (LTRA)**
  - Inhibits actions of leukotrienes

- **Theophylline**
  - Relaxes smooth muscle, may have mild anti-inflammatory effect
Controllers

- Inhaled corticosteroids-**first line therapy** for all levels of persistent asthma
- Use everyday even when asthma is well controlled
- Significantly lower side effect profile than oral steroids
- Do not work quickly and are not taken to relieve symptoms but are continued if symptoms develop
- May take several weeks of use to see full results
Inhaled Corticosteroids (ICS)

Q-var®
Flovent HFA®
Flovent Diskus®
Alvesco®
Asmanex®
Aerospan®
Pulmicort®
Inhaled Corticosteroids (ICS)

- Most effective anti-inflammatory therapy for persistent asthma
- Bind to glucocorticoid receptors in the cell to block many inflammatory processes
- Available in formulations for the nebulizer, MDIs, DPIs, and oral preparations
Beclomethasone (Q-var®)

- Available in doses of 40 or 80 mcg/puff
- Indicated for ages 5 and up
- Dosage 5-11 years 80 mcg to 160 mcg/day administered twice a day
- 12 years and up 80 mcg to >480 mcg/day administered twice a day
- Category C
Budesonide (Pulmicort®) Respules

- Available in doses of 0.25mg (green box) or 0.50mg (purple) or 1mg (black)
- **Maximum** recommended dose is 2 mg/day
  - administered once or twice a day
- Indicated for ages 12 months to 8 years
- Not to be used with ultrasonic nebulizers
- Suspension—must be gently mixed not shaken
- Generic vials may look different
- Category B
Budesonide (Pulmicort®) Flexhaler

- Available in 90 mcg and 180 mcg/puff
- Indicated for ages 5 years and older
- Dosage 180- >1200 mcg/day
- Category B
Ciclesonide (Alvesco®)

- Available in doses of 80 or 160 mcg/puff
- Indicated for ages 12 and up
- Dosage 80 to 320 mcg total daily dose
- Administered twice a day
- Dosage based on asthma severity
- Category C
Flunisolide (Aerospan™)

- Available in one strength 80 mcg/puff
- Indicated for ages 6 years and up
- Daily dose based on age
  - 6-11 160-320mcg/day
  - 12 and up 320-640mcg/day
- Administered twice a day
- Category C
Fluticasone Furoate (Arnuity®Ellipta®)

- Available in doses of 100 or 200 mcg/inhalation
- Indicated for ages 12 years and up
- Daily dose 100-200mcg/day
- Administered once a day
- Category C
Fluticasone Propionate (Flovent®) HFA/MDI

- Available in doses of 44 or 110 or 220mcg/puff
- Lowest recommended starting dose is 88 mcg BID
- Maximum recommended dose is based on age:
  - <4 years 176 mcg to >352 mcg
  - 5-11 years 88 mcg to >352 mcg
  - >12 years 88 mcg to >440 mcg
- Administered BID
- Category C
Fluticasone Propionate (Flovent®) DPI (diskus)

- Available in doses of 50 or 100 or 250 mcg/inhalation
- Indicated for ages 5 years and older
- Daily dose 100- >500 mcg/day
- Administered twice a day
- Category C
Mometasone (Asmanex®)

- Available as 110 or 220 mcg/puff
- Indicated for ages 4 and up
- Dosages 4-11 years: 110 mcg/day; ages 12 years up: 220- >440 mcg/day
- Approved for once daily dosing
- Category C
Combination Therapy

- Inhaled corticosteroid (ICS) plus Long acting Beta Agonist (LABA)
- Indicated for use if asthma not controlled with ICS alone
- Long acting beta agonist (LABA) added to ICS in one device
- LABAs should only be given with ICS NEVER alone when treating asthma
- Black box warning for all LABAs
Black Box Warning for Long Acting Beta Agonists (LABA)

- Long-acting beta2-adrenergic agonists (LABA), such as __________, one of the active ingredients in __________, increase the risk of asthma-related death. Data from a large placebo-controlled US trial that compared the safety of another LABA (salmeterol) with placebo added to usual asthma therapy showed an increase in asthma-related deaths in subjects receiving salmeterol. This finding with salmeterol is considered a class effect of LABA. Currently available data are inadequate to determine whether concurrent use of inhaled corticosteroids (ICS) or other long-term asthma control drugs mitigates the increased risk of asthma-related death from LABA. Available data from controlled clinical trials suggest that LABA increase the risk of asthma-related hospitalization in pediatric and adolescent patients.

- Therefore, when treating patients with asthma, physicians should only prescribe __________ for patients not adequately controlled on a long-term asthma control medication, such as an inhaled corticosteroid, or whose disease severity clearly warrants initiation of treatment with both an inhaled corticosteroid and a LABA. Once asthma control is achieved and maintained, assess the patient at regular intervals and step down therapy (e.g., discontinue __________) if possible without loss of asthma control and maintain the patient on a long-term asthma control medication, such as an inhaled corticosteroid. Do not use __________ for patients whose asthma is adequately controlled on low- or medium-dose inhaled corticosteroids [see Warnings and Precautions]
Budesonide and Formoterol (Symbicort®)

- Available in 80/4.5 and 160/4.5 per puff
- Indicated for ages 12 and up
- Dosed at 2 puffs twice a day
- Starting dose based on asthma severity
- Category C
Fluticasone Furoate and Vilanterol (Breo® Ellipta®)

- Available as 100/25 and 200/25
- 200/25 is for asthma
- Indicated for ages 18 and up
- One puff daily
- Category C
Fluticasone Propionate and Salmeterol (Advair®) HFA

- Available in 45/21, 115/21 and 230/21 per puff
- Indicated for ages 12 and up
- Dosed at 2 puffs twice a day
- Starting dose based on asthma severity
- Category C
Fluticasone Propionate and Salmeterol (Advair®) DPI

- Available in 100/50, 250/50 and 500/50 per puff
- Indicated for ages 12 and up
- Dosed at 1 puff twice a day
- Starting dose based on asthma severity
Mometasone and Formoterol (Dulera®)

- Available in 100/5 and 200/5/puff
- Indicated for ages 12 and up
- Dosage 2 puffs twice a day
- Starting dose based on asthma severity
- Category C
Leukotriene Modifiers

Leukotrienes

Inflammatory mediators produced in mast cells, eosinophils, basophils, leukocytes, macrophages

Primary role in the pathogenesis of inflammation
Leukotriene Modifiers

- Leukotriene modifiers (leukotriene antagonists) exerts anti-inflammatory effects and bronchodilatory response
- Block action of leukotrienes
- Step 2 alternate therapy ERP3 and GINA
- Magnitudes of anti-inflammatory effects are less than inhaled corticosteroids
Montelukast (Singulair®)

- Leukotriene Receptor Agonist (LTRA)
- Available in 4 mg, 5 mg and 10 mg
- Dosed on age not weight
- Granules 4 mg-mixed with food
- Chewable- 4 and 5 mg tablets
- Swallow -10 mg tablet

Side Effects
  - Nightmares
  - Headaches
  - GI upset
  - Psychiatric disorders
Zafirlukast (Accolate®)

- Available in 10 mg or 20 mg tablets
- Dosing for ages 5-11 years 10 mg PO BID
- For ages 12 years and up 20 mg PO BID
- Administer 1 hour before or 2 hours after meals
- Use with caution in patients on warfarin (P450 pathway)
- Requires monitoring of liver enzymes prior to starting and intermittently during treatment
- Category B
Zileuton (Zyflo CR®)

- 5- Lipoxygenase inhibitor
- Available as 600 mg tablets
- Indicated for ages 12 and up
- Dosage 1200 mg twice a day
- Administer 1 hour before or 2 hours after meals
- Use with caution in patients on warfarin (P450 pathway)
- Requires monitoring of liver enzymes prior to starting and intermittently during treatment
- Category C
Mast Cell Stabilizers

- Cromolyn sodium-Intal®
- Nedocromil-Tilade®
- No longer available in the U.S.A.
Other Controller Medications

- Anti-cholinergics
- Immunomodulators
- Methyxanthines
Spiriva® Respimat®

- Approved in 2015 for asthma in adults
- Recently approved for 6 and up
Steps to Load

1. Remove clear base (keep cap closed)
2. Insert cartridge
3. Replace clear base
4. Turn clear base in direction of arrows
5. Open cap
6. Press to prime
Steps to Use:

TOP  Turn Open Press

- Turn clear base with cap closed
- Open the cap until it snaps
- Exhale
- Place lips firmly around mouthpiece
- Press the dose release button while taking a slow, deep breath
- Hold breath for 10 seconds
- Close cap and repeat for second dose
IgE Inhibitors: Omalizumab (Xolair®)

- Recombinant, humanized monoclonal antibody, omalizumab selectively binds free IgE

- Omalizumab indirectly down-regulates the expression of FceRI receptors on basophils, mast cells, and dendritic cells, which may attenuate future allergic responses to allergens
IgE Inhibitors: Omalizumab (Xolair®)

- Omalizumab (Xolair®) binds to high affinity receptors on mast cells and basophil and low affinity receptor on macrophages, dendritic cells and B lymphocytes
- Patient must be poorly controlled on ICS
Indications

- Moderate to severe asthma
- With positive skin test or in vitro reactivity to perennial aeroallergen
- Symptoms not adequately controlled on inhaled corticosteroids (ICS)
- Patients 12 and up with allergic asthma (IgE between 30 and 700 and + test for perennial allergen)
New Xolair® Changes

- July, 2016: approved 6-11 year olds only for allergic asthma
- New serum IgE levels 30- 1300
- Weight: <44 or >330 lb
- Weight still a factor in dosing

March, 2015 approved for CIU for patients 12 and older
### Subcutaneous XOLAIR Doses Every 2 Weeks
#### Patients 12 Years of Age and Older With Asthma

<table>
<thead>
<tr>
<th>Body weight</th>
<th>Pounds</th>
<th>Kilograms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retreatment serum IgE (IU/mL)</td>
<td>66-132 lbs</td>
<td>&gt;132-154 lbs</td>
</tr>
<tr>
<td>30-60 kg</td>
<td>&gt;60-70 kg</td>
<td>&gt;70-90 kg</td>
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</tbody>
</table>

**Dose (mg):**
- ≥30-100
- >100-200
- >200-300
- >300-400
- >400-500
- >500-600
- >600-700
- DO NOT DOSE

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### Subcutaneous XOLAIR Doses Every 4 Weeks
#### Patients 12 Years of Age and Older With Asthma

<table>
<thead>
<tr>
<th>Body weight</th>
<th>Pounds</th>
<th>Kilograms</th>
</tr>
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</tr>
</tbody>
</table>

**Dose (mg):**
- ≥30-100
- >100-200
- >200-300
- >300-400
- >400-500
- >500-600
- >600-700
- See table on the left
### Table 3: Subcutaneous Xolair Doses Every 2 or 4 Weeks* for Pediatric Patients with Asthma Who Begin Xolair Between Ages of 6 to <12 Years

<table>
<thead>
<tr>
<th>Pre-treatment serum IgE (IU/mL)</th>
<th>Body weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20-25 kg</td>
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<tr>
<td><strong>Dosing Freq.</strong></td>
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<tr>
<td>Every 4 Weeks</td>
<td>75</td>
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<tr>
<td>Every 2 Weeks</td>
<td>150</td>
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</tbody>
</table>

*DO NOT DOSE*

*Dosing Frequency:*
- Green: Subcutaneous doses to be administered every 4 weeks
- Light blue: Subcutaneous doses to be administered every 2 weeks
Omalizumab (Xolair®)

- An immunomodulator-Anti-IgE preparation administered sub-cutaneously
- For patients with moderate to severe asthma
- Pediatric indication July, 2016
- Dosage based upon weight and IgE level
- Administered every 2-4 weeks
- Patient 12 and older must have allergy to perennial aeroallergen, IgE level of 30-700 IU/mL and asthma inadequately controlled by ICS therapy
- Approved June, 2003
Interlukin-5 (IL-5)

- Major cytokine responsible for eosinophil development
- Responsible for maturation and release of eosinophils in the bone marrow
- Selective cytokine restricting expression to IL-5 receptors on eosinophils and basophils
- Binds to IL-5 receptor complex expressed on the eosinophil surface
Interlukin-5 (IL-5)

Eosinophil phenotype associated with:

- compromised lung functions
- more frequent symptoms
- increased risk of exacerbations
Anti-IL-5—Mepolizumab (Nucala®)

- Humanized monoclonal antibody
- Mechanism of action is not definitively established
- Targets eosinophils prevents IL-5 binding to receptor
- Approved November, 2015
Anti-IL-5—Mepolizumab (Nucala®)

- Indicated for add-on maintenance treatment of patients with severe asthma age 12 and older and with an eosinophilic phenotype
- Eosinophil ≥ 150 cell/µL within 6 weeks of dosing OR ≥ 300 µL within 12 months
- No requirements for IgE levels
- Dosage 100 mg administered subcutaneously once every 4 weeks regardless of weight
Anti-IL-5—Mepolizumab (Nucala®)

- Total of 1,327 subjects evaluated in 3 randomized, placebo-controlled multicenter trials of 24 to 52 weeks duration (Trials 1, 2 and 3)
- In trials 1 & 2 (n=1,192) subjects had a history of 2 or more exacerbations in the year prior to enrollment despite regular use of high-dose ICS plus and additional controller
- In trial 3 (n=135) subjects required daily oral steroids in addition to high-dose ICS and additional controller
Adverse events ≥3% and More Common than Placebo

- Headache
- Injection site reaction
- Back pain
- Fatigue
- Influenza
- UTI
- Upper abdominal pain
- Pruritus
- Eczema
- Muscle spasms
Long Term Safety

- 998 subjects have received Nucala in ongoing open-label studies during which additional cases of herpes zoster have been reported.
- 15/260 subjects developed anti-mepolizumab antibodies.
- Pregnancy:
  - Exposure registry [www.mothertobaby.org/asthma](http://www.mothertobaby.org/asthma)
  - Not teratogenic in mice
  - No adverse effect on fetal or neonatal growth in monkeys.
Outcomes

- 53% reduced exacerbations
- Greater reduction of oral corticosteroid use
- No change in FEV1

http://www.nucala.com/
Anti-IL-5 Reslizumab (Cinqair™) (Previously Cinqunil)

- Humanized IL-5 antagonist monoclonal antibody (IgG4 kappa)
- Add-on maintenance treatment now available for patients 18 years and older with severe asthma and the eosinophilic phenotype
- Reslizumab reduces severe asthma by lowering blood levels of eosinophils
- Approved December, 2015
Anti-IL-5 Reslizumab (Cinqair™) (Previously Cinqquil)

Peripheral blood eosinophil ≥ 400 cmL within the previous 4 weeks

AND

Three consecutive months of ICS/LABA therapy
Anit-IL-5 Reslizumab (Cinqair™) (Previously Cinquil)

Recommended dosing:

3 mg/kg once every four weeks by IV infusion over 20 – 50 minutes

Available as 100 mg single-use 10 ml vials
Anit-IL-5 Reslizumab (Cinqair™) (Previously Cinquirl)

- Total of 981 subjects evaluated in 4 randomized, placebo-controlled studies 16 to 52 weeks in duration
- In trials 1 & 2 (n=953) subjects had blood eosinophil count of at least 400 mcL, on medium-high dose ICS plus LABA
- Patients on OCS at baseline was 11%
- Trials 1 & 2 were 52 weeks duration
Anit-IL-% Reslizumab (Cinqair™)

- Study 3 (n=315) required blood eosinophil count of at least 400 mcL, no OCS. No notation of ICS dose.
- Study 4 (n=496) no requirement for blood eosinophils but 80% of subject had a screening with eos count of < 400 and OCS not allowed. No notation of ICS dose.
Adverse events

- Anaphylaxis—Cinqair 0.6%; placebo 0.3%
- Malignancy—Cinqair 0.6%; placebo 0.3%
- No other adverse events listed
Outcomes

- Fewer exacerbations
- Reduced need for OCS
- Fewer ED visits
- Fewer hospitalizations
Theophylline

- A methylxanthine
- Available as a liquid, tablet, capsule and sustained release tablet preparations
- Starting dose 10 mg/kg/day adjust dose to achieve serum level of 5-15 mcg/ml
- High level of risk for overdose, interacts with many other medications
- Typically used only be specialists to manage severe asthma
Medications to Treat Allergic Rhinitis

- Poorly controlled AR can contribute to poorly controlled asthma
- Inhaled Nasal Steroids (INS) are first line treatment for allergic rhinitis
- Anticholinergic nasal sprays are sometimes added to INS therapy for excess nasal secretions
- Nasal antihistamines are also used
Inhaled Nasal Steroids

- Flunisolide (Nasonex®)
- Fluticasone (Flonase® and Veramyst®)
- Beclomethasone (Q-Nasl®)
- Budesonide (Rhinocort®)
- Ciclesonide (Omnaris® and Zetona®)
- Mometasone (Nasonex®)
- Triamcinolone (Nasacort AQ®)
Other Nasal Sprays

- Anticholinergic—Ipatropium (Atrovent®)
- Antihistamine—Azelastine (Astelin® and Astepro®); Olpatadine (Patanase®)
- Antihistamine and Fluticasone (Dymista®)
Instructions for Nasal Sprays

- Shake gently
- Remove cap
- Blow nose
- Tip head forward
- Insert tip of applicator into the nostril
- Use opposite hands to administer
- Spray once in each nostril, breath out through the mouth
- Repeat if dose requires
- For antihistamines gently massage nose after dosing
Relievers

Albuterol

Ventolin®

ProAir HFA®

ProAir RespiClick®

Levalbuterol

Proventil®

Xopenex®
Relievers

- Reliever NOT rescue
- Meant to be used quickly to relieve symptoms of asthma
- Should be used at first sign of symptoms
- If asthma is well controlled, should not be needed more than twice a week during the day or twice a month at night
- Do not count doses used prior to exertion to prevent EIB
Albuterol (Proventil®, Ventolin®, ProAir®)

- 90 mcg/puff
- Indicated for ages 4 and up
- Dose 2 puffs every 4-6 hours for relief of symptoms; 2 puffs 15 minutes prior to exertion to prevent EIA
Albuterol (ProAir® Respiclick)

- 90mcg/puff
- Indicated for ages 12 and up
- Dose 2 puffs every 4-6 hours for relief of symptoms; 2 puffs 5 minutes prior to exertion to prevent EIA
Levalbuterol (Xopenex®)

- 45 mcg/puff
- Indicated for ages 4 and up
- Dose 2 puffs every 4-6 hours for relief of symptoms; 2 puffs 15 minutes prior to exertion to prevent EIA
- 1 puff may be sufficient in some patients
Nebulized Relievers

- Albuterol 2.5 mg per vial
- Levalbuterol (Xopenex®) 1.25 mg, 0.63 mg, 0.31 mg
- Ipatropium (Atrovent®) 250 mg per vial
- Administered by mask or mouthpiece via nebulizer
- NO BLOW-BYs
Ipratropium Bromide (Atrovent®)

- Anticholinergic
- Available as MDI and nebulizer solution
- Approved for ages 12 and up
- EPR III recommended usage for asthma is 4-8 puffs or 500 mg (via nebulizer) with selective SABA in the ED
- Not recommended for prolonged use due to lack of evidence to support efficacy
Other Relievers

- Prednisone
- Prednisolone
- Methylprednisolone
- Injectable steroids

- Given for short periods of time for exacerbations
- Inhaled steroids should be started at the same time if patient not already on ICS
Oral Systemic Corticosteroids

- Dosing for short bursts is 1-2 mg/kg/day to maximum dose of 60 mg
- Given once a day or split and given twice a day
- Typically given for 3-10 days
- Should be taken with food
Asthma Medications
Inhaled Corticosteroids vs Oral

- Typical pediatric oral burst for 15 kg. child at 2 mg/kg
  - Prednisolone 15 mg po bid for 5 days = 150 mg/burst
  - 150 mg = 150,000 mcg

- Low dose ICS
  - Fluticasone 44 mcg 2 puffs bid = 176 mcg/day
  - If adjusted for ~15% bioavailability = 26.4 mcg/day (176 x 0.15 = 26.4)

- \[ 150,000 \div 26.4 = 5,681 \text{ days OR 15.56 years} \]
  - of ICS to equal one oral burst
Medications that may worsen asthma

Beta blockers

- Medications prescribed to treat numerous conditions including heart conditions, high blood pressure, migraine headache, and, in eye drop form, glaucoma.
- Risk of reducing the effect of bronchodilation effect of albuterol.
- Examples: labetalol, propranalol, timolol ophthalmic drops
Medications that may worsen asthma

ACE inhibitors

- Medications prescribed to treat hypertension (high blood pressure), heart failure, acute myocardial infarction (heart attack), and proteinuria in IgA nephropathy.
- ACE inhibitors may cause dry, hacking, nonproductive cough that usually occurs within the first few months of treatment and should generally resolve within 1-4 weeks after discontinuation of the ACE inhibitor. Should consider other causes of the cough (i.e. pulmonary congestion as in heart failure).
- Examples: lisinopril, captopril, other “–pril” drugs
Medications that may have undesired side effects

SSRIs (selective serotonin reuptake inhibitors)

- Medications prescribed to treat depression, anxiety, OCD, and other psychiatric conditions
- Some SSRIs may cause QTc prolongation (dysrhythmia) depending on dose. Beta-agonists (i.e. albuterol) may produce ECG changes (flattening of the T wave, prolongation of the QTc interval, ST segment depression).
- Examples: Prozac, Lexapro, Celexa