Pediatric Asthma Medication Update

Elizabeth Melville Klements, MS, RN, PPCNP-BC, AE-C
Asthma Clinical Practice Specialist
Pediatric Nurse Practitioner

Disclosures

- I have no conflicts of interest
- I have no relevant financial disclosures
Learning Objectives

- Describe key changes in NHLBI 2020 guidelines
- Describe key consideration for choosing the proper medication/s when treating children with asthma.
- Discuss criteria for starting children with asthma on biologics.

Basic Physiology

- Hyper-responsiveness of the airways
- Bronchoconstriction
- Inflammation
  - Increased mucous production

- This is key to your teaching, and patient understanding of the need for bronchodilators and anti-inflammatories
Assessing Asthma Severity: Impairment

Impairment = Frequency and Intensity of Symptoms and Functional Limitations

- **Symptoms**
  - Nighttime awakenings
  - Need for albuterol
  - Missed School days
  - Ability to be active
  - QOL assessments

- **Lung Function**
  - Spirometry
  - Peak flow

Assessing and Reducing Risk of Asthma Exacerbations

- Prevent recurrent exacerbations of asthma and minimize the need for ED visits or hospitalizations.
- Prevent loss of lung function; for children, prevent reduced lung growth.
- Provide optimal pharmacotherapy with minimal or no adverse effects of therapy.
Assessing asthma care

• What medications are you taking?
• How do you take them?
• Is the technique correct?
• Are there other factors contributing to asthma?
  • Multiple caregivers
  • Environmental triggers
  • Co-morbidities

What we’ve learned since 2007:

• Long-acting muscarinic antagonists (LAMAs) are safe with ICS (Inhaled Corticosteroids)
• Formoterol is a quick acting LABA (long-acting beta-agonist) that can be used for rescue/quick relief
• LAMAs are effective bronchodilators for asthma (as they have been for COPD)
• Biologics are effective in severe allergic/eosinophilic asthma
### Updates to 0-4 year old step algorithm

**Management of Persistent Asthma in Individuals Ages 0-4 Years**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>STEP 1</th>
<th>STEP 2</th>
<th>STEP 3</th>
<th>STEP 4</th>
<th>STEP 5</th>
<th>STEP 6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preferred</strong></td>
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<td>Daily medium-dose ICS LA, ICS LABA and PRR SABA</td>
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*Key Changes*
- Intermittent (7-10d course) ICS in step 1 for RTI (respiratory tract infection) wheezers without intercurrent wheezing

### Updates to 5-11 year old step algorithm

**Management of Persistent Asthma in Individuals Ages 5-11 Years**

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<td><strong>Alternative</strong></td>
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*Key Changes*
- Patients with mild-moderate asthma and adherent to daily ICS do NOT increase ICS for increased symptoms
- SMART (ICS-Formoterol) preferred for step 3 & 4, not to exceed 8 Puffs/24hr
Updates to ≥12 year old step algorithm

Key Changes
Patients with mild-moderate asthma and adherent to daily ICS do NOT increase ICS for increased symptoms
SMART (ICS-Formoterol) preferred for step 3 & 4, not to exceed 12 Puffs/24hr
LAMA may be added to ICS if LABA not an option (Step 4 alternative).
Caution of potential increased Asthma Exacerbation in Blacks.
LAMA should be added to ICS-LABA (step 5) for improved control/quality of life.

Implementation uncertainty regarding SMART (Single Maintenance and Relief Therapy) therapy

- Currently SMART therapy is not FDA approved
- Insurance obstacles may exist to providing sufficient quantity of ics-formoterol inhalers to support SMART therapy
- Potential overuse/underuse requires careful monitoring
  – Need to be careful with high and low symptom perceivers
- Provider and patient preference and education
Medication Categories

Quick-Relief Medication for All Patients

- Albuterol as needed for symptoms.
- With URI: Albuterol q 4-6 hours up to 24 hours. See provider if using greater than 3 days. Consider short course of oral systemic corticosteroids.
- Frequent use of Albuterol may indicate the need to step up treatment to initiating or increasing daily long-term-control therapy.
**Quick Relievers**

- Albuterol
- ProAir
  - HFA
  - RespiClick
  - Digihaler (App to track usage)
- Proventil
- Ventolin
- Levalbuterol
  - Xoponex—3 x the price of albuterol

**Long-Term Control**

- Taken daily, over a long period of time
- Used to reduce inflammation, relax airway muscles, and improve symptoms and pulmonary function

- Inhaled corticosteroids
- Long-acting beta2-agonists (LABA)
- Long-acting Muscarinic Antagonist (LAMA)
- Leukotriene modifiers
- Biologics
Inhaled Corticosteroids

- Budesonide DPI (Pulmicort) 90, 180 mcg/puff
- Mometasone MDI-HFA (Asmanex) 50, 100, 200 mcg/puff
- Mometasone DPI (Asmanex Twisthaler) 110, 220 mcg/puff
- Beclomethasone MDI-HFA (QVAR) 40, 80 mcg/puff
- Fluticasone MDI-HFA (Flovent) 44, 110, 220 mcg/puff
- Fluticasone DPI (Flovent Discus) 50, 100, 250 mcg/puff
  - (ArmonAir Respiclick) 55, 113, 232 mcg/puff
- Fluticasone furoate DPT (Arnuity) 100, 200 mcg/puff
- Ciclesonide MDI-HFA (Alvesco) 80, 160 mcg/puff

Dry Powder Inhalers
Fluticasone furoate (Arnuity Ellipta)

- Once daily therapy
- Dry Powder
- Available in 100mcg and 200mcg
- Approved for ≥ 12 years old

Budesonide is the only nebulized corticosteroid
Benefits of Inhaled Steroids

- Improved lung function
- Decreased hyper-responsiveness
- Fewer asthmatic symptoms
- Reduce use of quick relief medications
- Improved health related quality of life
- Decreased risk of death or near death from asthma

Adverse Effects of Corticosteroids

- Oral candidiasis (thrush)
- Hoarse voice (dysphonia)
- Medium to high dose inhaled steroids associated with small effect on linear growth (1cm) during first year
Combination Therapy

• Good for patients with poorly controlled asthma on inhaled corticosteroids

• Good for patients with nighttime symptoms

• Now recommended as SMART therapy in mild – moderate asthma as a prn dose in place of SABA. Although not FDA approved yet.

Long Acting Beta Agonists

- Salmeterol (Serevent)
- Formoterol (Foradil)
- Vilanterol (In Breo Ellipta)

- Not recommended:
  - Oral beta-agonists (Volmax, Vospire ER)
Long Acting Beta Agonists

- Relax bronchial smooth muscle
- Available as DPI
- 12 or 24 hour duration of action
- Most effective when in combination with inhaled steroids (not mono therapy)
- Effective control for nocturnal symptoms

Combination Inhaled Corticosteroid & Long Acting Beta Agonist

**Advair**
- Fluticasone/Salmeterol
- MDI or Discus
- Approved for ≥ 4 years

**Wixela**
- Fluticasone/Salmeterol
- Dry powder “Inhub” device
- Approved for ≥ 4 years

**Symbicort (SMART therapy)**
- Budesonide/Formoterol
- MDI – requires a spacer
- Approved for ≥ 12 y.o

**Dulera (SMART therapy)**
- Mometasone/Formoterol
- Approved for ≥ 12 olds

**Breo Ellipta**
- Fluticasone furoate/vilanterol
- Approved for ≥ 18 year olds
Newest Dry Powder Combination Inhaler

- Breo Ellipta
- Approved for ages 18 and older
- Once every 24-hour dosing
- Originally for COPD

Long-acting Muscarinic Antagonist Tiotropium (Spiriva Respimat)

- Usually 2 sprays once daily, must be used regularly to be effective
- Approved for patients ≥ 6 years
- Anticholinergic - works by relaxing the muscles around the airways so that they open up and you can breathe more easily
- It does not work right away and should not be used to relieve sudden symptoms
Triple Therapy Inhaler

- Trelegy Ellipta
- Fluticasone, umeclidinium & vilanterol
- Once Daily
- Approved for 18+

Another Combination Inhaler Combivent

- Albuterol and Atrovent combined
- Used in ED and ICU commonly
- May be prescribed by specialists
Warning – Do Not Use Primatene Mist (Epinephrine)

- Primary utility is in acute anaphylaxis with edema; not recommended for routine management and treatment of asthma (GINA 2020; NAEPP 2007).
- Over the counter
- ~ $35

Leukotriene Modifiers
Leukotriene Modifiers

- Montelukast (Singulair) – Once daily tablet, chewable, & sprinkles
  - Approved for ages ≥ 1 year
  - 4 mg, 5 mg, 10 mg
- Zafirlukast (Accolate) – Twice daily tablet
  - Ages ≥ 5 year
  - Requires routine monitoring of Liver function
- Zileuton (Zyflo) – BID or QID
  - ≥ 12 years
  - Requires routine monitoring of Liver function

Montelukast

Black Box Warning

- Serious neuropsychiatric (NP) events have been reported with the use of montelukast. The types of events reported were highly variable, and included, but were not limited to, agitation, aggression, depression, sleep disturbances, suicidal thoughts and behavior (including suicide). The mechanisms underlying NP events associated with montelukast use are currently not well understood.
- Because of the risk of NP events, the benefits of montelukast may not outweigh the risks in some patients, particularly when the symptoms of disease may be mild and adequately treated with alternative therapies. Reserve use of montelukast for patients with allergic rhinitis who have an inadequate response or intolerance to alternative therapies. In patients with asthma or exercise-induced bronchoconstriction, consider the benefits and risks before prescribing montelukast.
- Discuss the benefits and risks of montelukast with patients and caregivers when prescribing montelukast. Advise patients and/or caregivers to be alert for changes in behavior or new NP symptoms when taking montelukast. If changes in behavior are observed, or if new NP symptoms or suicidal thoughts and/or behavior occur, advise patients to discontinue montelukast and contact a health care provider immediately.
Leukotriene Modifiers

- 1/3 patients respond well
- 1/3 respond somewhat,
- 1/3 do not respond
- May be used as alternative or adjunct to inhaled steroids

When to use Leukotriene Blocking Drugs

- Patients with severe asthma on high-dose inhaled steroids
- Steroid dependent asthma
- Mild to moderate asthma in persons fearful or intolerant of inhaled steroids
How to make the selection?

- Nebulized medications
  - No blow by treatments!
- Metered Dose inhalers
  - Must use a valved holding chamber (spacer)
- Dry power inhalers
  - Can child hold his/her breath and swim under water?

Good Rx App

- Free App on smart phones
- Shows prescription prices at local pharmacies
- Provides coupons when available
Biologics

Checklist of Steps to Consider Prior to Biologic Therapy for Severe Asthma

1. Verify patients are adherent and are using standard therapies appropriately.
2. Address all co-morbidities that can impair asthma control including rhinitis, nasal polyposis, sleep apnea, and GERD.
3. Evaluate and assess triggers of asthma specific to the patient, such as drugs, tobacco smoke, and allergens.
4. Optimize alternative controller medications other than inhaled corticosteroids and bronchodilators, such as leukotriene pathway modifiers.
5. Verify presence of prerequisite indications for monoclonal antibodies (e.g. positive skin tests and total IgE between 30 and 700 IU/ml for omalizumab or eosinophilia for IL-5 inhibitors).
Biologics

- For patients with severe persistent asthma who do not respond well to other treatments
- Only ~60-70 of our 10,000 patients receive this medicine.

Omalizumab (Xolair)

- Binds free IgE & inhibits its binding to mast cell
- Reduces early & late allergic responses
- Reduces exacerbations 50% (moderate and severe asthma)
- Expensive ($10-30k/year)
- Given every 2-4 weeks depending on IgE level and weight
- May have delayed anaphylactic response, so must have epi-pen on hand
Who qualifies for Xolair

- 6 years or older
- Moderate or Severe Persistent Asthma
- Daily asthma symptoms
- 2 or more asthma attacks/week
- Positive skin test or blood test for allergies
- Symptoms even on inhaled steroids
- IgE levels are 30-1300 IU/ml
- Body weight 40-330 lbs.

Mepolizumab (Nucala)

- Add-on maintenance treatment
- ≥ 6 years old, with severe Eosinophilic asthma
- Reduces blood eosinophils, which may contribute to asthma
- Trials show it Effectiveness in Nasal Polyps
- Reduces steroid use
- Take at home option for patients 12+
- Costs $3000 - $6500/dose (monthly)
**Dupilumab (Dupixent)**

- Maintenance treatment of moderate to severe asthma &/or Atopic dermatitis
- Anti-eosinophils
- Every 2 week, SQ administration
- May be self administered at home
- Patients 6 or older who are not well controlled on their current medications
- May be self-administered at home
- Originally approved for atopic dermatitis

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**Benralizumab (Fasenra)**

- Binds to eosinophils
- Approved for ages ≥ 12
- Given every 4 weeks for first 3 months
- Then only needs to be administered every 8 weeks
- May be self-administered by patients after proper instruction
- Costs $5000-$7300/ dose
Reslizumab (Cinqair)

- Add-on maintenance treatment
- ≥ 18 years old, with severe asthma
- Reduces blood eosinophils, which may contribute to asthma
- IV infusion, 3 mg/kg, every 4 weeks, over 25-50 minutes

Asthma Resources

- [www.bostonchildrens.org/asthmavideos](http://www.bostonchildrens.org/asthmavideos)
- 19 Asthma Family Education Sheets
- 16 Instructional videos in English and Spanish