Navigating the Roadmap for Treating Pediatric Asthma: Latest Guidelines and Strategies

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Sanford Children’s, Pediatric Pulmonology

Speaker Introduction

- Dr. Deb Hickman practices at Sanford Children’s Pulmonary Clinic in Sioux Falls, S.D. with a primary focus in asthma. Patients come from a five-state rural referral area, including outreach clinics and telemedicine. She obtained her BSN from the University of Iowa, neonatal nurse practitioner certificate and MSN from South Dakota State University, a post master’s Primary PNP certificate from St. Louis University and a DNP from South Dakota State University. She is a clinical faculty member of the Sanford USD School of Medicine. Dr. Hickman chairs the Asthma and Allergy SIG. She is an advisory member for the South Dakota Board of Nursing. A long time champion for advanced practice nursing, she is leading standardization of advanced practice onboarding across the Sanford enterprise. She is chair of the Sanford Sioux Falls Advanced Practice Council and member of the Physician Executive Council, Clinical Practice Committee, Professional Health Practice Committee, and Advanced Practice Credentialing Committee.

Disclosures

Financial relationships:
I have no financial relationships to disclose related to this presentation

Off-label use of medications:
Newer asthma guidelines include off-label use of medications

Learning Objectives

- Review the evidence behind new strategies for the treatment of asthma
- Discuss the latest available clinical guidelines for the treatment of pediatric asthma
- Identify differences between current clinical guidelines and FDA-approved use of asthma medications in order to make informed plans of action for your patients with asthma

What is new since 2007?

- Symbicort 1:1 (2010)
- Symbicort 9:1 (2007)
- Symbicort 6:1 (2017)
- Spiriva 6mcg (2010)
- Spiriva 12mcg (2011)
- Kerlina discus delivery
- Advair

Components of Asthma

- Chronic Inflammation
- Airways Obstruction
- Clinical Asthma Symptoms
- Asthma Flare (Exacerbations)

GINA 2019
NAEP 2020 (coming)
Hot topics and latest evidence

- The clinical utility of fractional exhaled nitric oxide (FeNO) in asthma management
- Effectiveness of indoor allergen reduction in management of asthma
- Role of immunotherapy in the treatment of asthma
- Intermittent inhaled corticosteroids and long-acting muscarinic antagonist for asthma

Latest evidence: The diagnostic accuracy of FeNO


<table>
<thead>
<tr>
<th>FeNO cutoff</th>
<th>Age Group</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Diagnostic Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20 ppb</td>
<td>&gt;18 years</td>
<td>0.80</td>
<td>0.64</td>
<td>7.28</td>
</tr>
<tr>
<td>&lt;18 years</td>
<td>0.78</td>
<td>0.89</td>
<td>13.44</td>
<td></td>
</tr>
<tr>
<td>20-29 ppb</td>
<td>&gt;18 years</td>
<td>0.69</td>
<td>0.78</td>
<td>7.70</td>
</tr>
<tr>
<td>&lt;18 years</td>
<td>0.61</td>
<td>0.89</td>
<td>12.13</td>
<td></td>
</tr>
<tr>
<td>30-39 ppb</td>
<td>&gt;18 years</td>
<td>0.53</td>
<td>0.85</td>
<td>6.27</td>
</tr>
<tr>
<td>&lt;18 years</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>≥40 ppb</td>
<td>&gt;18 years</td>
<td>0.41</td>
<td>0.93</td>
<td>9.84</td>
</tr>
<tr>
<td>18 years</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

ATS Clinical Practice Guideline FeNO-2011

Dweik et al. (2011). An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FeNO) for clinical applications. American Journal of Respiratory and Critical Care Medicine, 184(5): 602-15

- > 18 years: <25 ppb and >50 ppb are the most useful cutoffs
- < 18 years: <20 ppb and >35 ppb are the most useful cutoffs
- FeNO is an indirect test for airway inflammation which may aid in:
  - Detection of eosinophilic airway inflammation
  - Determine the likelihood of corticosteroid responsiveness
  - Monitoring airway inflammation
  - Unmasking otherwise unsuspected non-adherence to corticosteroid therapy

Conclusions

- May be more predictive in children (5 years of age and older)
- Not found to be a helpful predictor in children ages 0-4 years
- FeNO is useful as an adjunct diagnostic test ≥ 5 years of age
- to aid in diagnosis
  - ongoing asthma monitoring and management of patients with persistent asthma
- No definitive cut-off values
- Negative FeNO does not exclude asthma
- No clinical utility if used in isolation to monitor and manage persistent asthma.
  - Should be used only as a second line test

Indoor allergen reduction in management of asthma


Studies reviewed: 58 RCT, 8 non-randomized trials
**Single indoor allergen mitigation strategies**

Leas et al. (2018)

<table>
<thead>
<tr>
<th>Single interventions: 37 studies</th>
<th>Asthma control</th>
<th>Exacerbation</th>
<th>Healthcare use</th>
<th>Absenteeism</th>
<th>Pulmonary physiology</th>
<th>Quality of life</th>
<th>Symptoms</th>
<th>Allergen reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acaricide</strong></td>
<td>NA</td>
<td>Inconclusive</td>
<td>NA</td>
<td>NA</td>
<td>Improved</td>
<td>NA</td>
<td>NA</td>
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</tr>
<tr>
<td><strong>Air purification</strong></td>
<td>NA</td>
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<td>Improved</td>
<td>NA</td>
<td>Inconclusive</td>
<td>Improved</td>
</tr>
<tr>
<td><strong>Carpet removal</strong></td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Inconclusive</td>
<td>NA</td>
<td>NA</td>
<td>Inconclusive</td>
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<tr>
<td><strong>HEPA vacuums</strong></td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Inconclusive</td>
<td>NA</td>
<td>NA</td>
<td>Inconclusive</td>
</tr>
<tr>
<td><strong>Mattress covers</strong></td>
<td>Inconclusive</td>
<td>NA</td>
<td>Inconclusive</td>
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<td>Inconclusive</td>
<td>NA</td>
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<td>Inconclusive</td>
</tr>
<tr>
<td><strong>Mold removal</strong></td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<td>NA</td>
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</tr>
<tr>
<td><strong>Pet control</strong></td>
<td>Inconclusive</td>
<td>NA</td>
<td>Inconclusive</td>
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<td>Inconclusive</td>
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</tbody>
</table>

*No clear evidence to demonstrate the most effective single or multicomponent indoor allergen mitigation interventions on asthma outcomes*

**Multicomponent indoor allergen mitigation strategies**

Leas et al. (2018)

<table>
<thead>
<tr>
<th>Multicomponent interventions: 30 studies</th>
<th>Asthma control</th>
<th>Exacerbation</th>
<th>Healthcare use</th>
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<th>Pulmonary physiology</th>
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<td>NA</td>
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<td>NA</td>
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</tr>
<tr>
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<td>Inconclusive</td>
<td>NA</td>
<td>NA</td>
<td>Improved</td>
</tr>
</tbody>
</table>

**Role of immunotherapy in the treatment of asthma**

Lin et al. (2018)

- Studies on the efficacy of subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT)
- 31 SCIT efficacy trials
- 18 SLIT efficacy trials
- Health outcomes studied
  - Asthma symptoms
  - Quality of life
  - Quick-relief medication use
  - Long-term control medication use
  - Systemic steroids
  - Health care use
  - FEV1

<table>
<thead>
<tr>
<th>Outcome</th>
<th>SCIT</th>
<th>SLIT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma symptoms</td>
<td>Insufficient</td>
<td>Improves ACT (high SOE)</td>
</tr>
<tr>
<td>Quality of life</td>
<td>Improves (low SOE)</td>
<td>Improves (low SOE)</td>
</tr>
<tr>
<td>Quick-relief medication use</td>
<td>Reduces use (low SOE)</td>
<td>Reduces use (low SOE)</td>
</tr>
<tr>
<td>Long-term control medication use</td>
<td>Reduces need (moderate SOE)</td>
<td>Reduces need (moderate SOE)</td>
</tr>
<tr>
<td>Systemic steroids</td>
<td>Reduces use (low SOE)</td>
<td>Insufficient</td>
</tr>
<tr>
<td>Health care use</td>
<td>Insufficient</td>
<td>Insufficient</td>
</tr>
<tr>
<td>FEV1</td>
<td>Increases (low SOE)</td>
<td>Improves (moderate SOE)</td>
</tr>
</tbody>
</table>

**Allergen-specific immunotherapy in the treatment of pediatric asthma**

Rice et al. (2018)

- 40 studies (≤18 years of age) on the safety and efficacy of subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT)
- 17 SCIT trials
- 11 SLIT trials
- 8 non-RCT for SLIT safety
- 4 non-RCT for SCIT safety
- Health outcomes studied
  - Asthma symptoms
  - Quality of life
  - Quick-relief medication use
  - Long-term control medication use
  - Systemic steroids
  - Health care use
  - FEV1
Outcomes on effects of allergen specific immunotherapy on treatment of asthma (pediatric)- Rice et al. (2018).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>SCIT</th>
<th>SLIT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma Symptoms</td>
<td>Insufficient</td>
<td>No studies</td>
</tr>
<tr>
<td>Quality of life</td>
<td>Improves (low SOE)</td>
<td>No studies</td>
</tr>
<tr>
<td>Quick-relief medication use</td>
<td>May reduce use? (low SOE)</td>
<td>No effect (low SOE)</td>
</tr>
<tr>
<td>Long-term control medication use</td>
<td>Reduces use (moderate SOE)</td>
<td>No effect (low SOE)</td>
</tr>
<tr>
<td>Systemic steroids</td>
<td>May reduce use? (low SOE)</td>
<td>Insufficient: One study shows may reduce use</td>
</tr>
<tr>
<td>Health care use</td>
<td>Insufficient</td>
<td>No studies</td>
</tr>
<tr>
<td>FEV1</td>
<td>Improves (low SOE)</td>
<td>No studies</td>
</tr>
</tbody>
</table>

Conclusions
- **Adults**
  - SCIT: Reduces use of long-term control medications
  - May improve asthma related quality of life and FEV1
  - May reduce the use of SABA
  - May reduce need for systemic corticosteroids.
- **SLIT**: Improves asthma symptoms
  - Improves quality of life
  - Reduces need for long-term control medications
  - May reduce the use of SABA
  - Insufficient evidence for use in children
- **Pediatrics**
  - SCIT: reduces use of long-term control medications
  - May improve asthma related quality of life and FEV1
  - SLIT: May improve medication use and FEV1

Intermittent inhaled corticosteroids and long-acting beta agonists as controller and quick relief therapy for asthma

The following is off-label use:
- As needed ICS
- As needed ICS/formoterol

**Daily Inhaled Corticosteroids**

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Age 3 yrs-6 yrs</th>
<th>Age 6-11 yrs</th>
<th>Age 12 yrs and older</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asmanex 100 mcg</td>
<td>110</td>
<td>220</td>
<td>110-220</td>
</tr>
<tr>
<td>Asmanex 200 mcg</td>
<td>≥220</td>
<td>&gt;440</td>
<td>&gt;440</td>
</tr>
<tr>
<td>Asmanex Twisthaler 110 mcg</td>
<td>4+</td>
<td>12+</td>
<td>12+</td>
</tr>
<tr>
<td>Flovent 50 mcg</td>
<td>50</td>
<td>NA</td>
<td>100</td>
</tr>
<tr>
<td>Flovent 100 mcg</td>
<td>100</td>
<td>NA</td>
<td>200</td>
</tr>
<tr>
<td>Flovent 250 mcg</td>
<td>250</td>
<td>&gt;250</td>
<td>&gt;250</td>
</tr>
<tr>
<td>Alvesco 80 mcg</td>
<td>80</td>
<td>&gt;80</td>
<td>&gt;80</td>
</tr>
<tr>
<td>Alvesco 160 mcg</td>
<td>&gt;160</td>
<td>&gt;160</td>
<td>&gt;160</td>
</tr>
<tr>
<td>Pulmicort 100 mcg</td>
<td>100</td>
<td>&gt;100</td>
<td>&gt;100</td>
</tr>
<tr>
<td>Pulmicort 250 mcg</td>
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<td>&gt;250</td>
<td>&gt;250</td>
</tr>
<tr>
<td>Qvar 40 mcg</td>
<td>40</td>
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<td>Qvar 80 mcg</td>
<td>&gt;80</td>
<td>&gt;80</td>
<td>&gt;80</td>
</tr>
<tr>
<td>Beclomethasone HFA 50 mcg</td>
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<td>100</td>
</tr>
<tr>
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<td>NA</td>
<td>200</td>
</tr>
<tr>
<td>Beclomethasone HFA 250 mcg</td>
<td>250</td>
<td>&gt;250</td>
<td>&gt;250</td>
</tr>
<tr>
<td>Ciclesonide HFA 80 mcg</td>
<td>80</td>
<td>&gt;80</td>
<td>&gt;80</td>
</tr>
<tr>
<td>Ciclesonide HFA 160 mcg</td>
<td>&gt;160</td>
<td>&gt;160</td>
<td>&gt;160</td>
</tr>
</tbody>
</table>

*Note: Data are from the Summary of Product Characteristics of medicines withnil, and the evidence for use in children was based on sound scientific evidence, expert medical judgement, or published literature. BAI: Breath Actuated Inhaler DPI: Dry Powder Inhaler MDI: Meter Dose Inhaler*
Combination Inhaled Corticosteroid (ICS) + Long acting beta 2 agonist (LABA) Controllers

<table>
<thead>
<tr>
<th>Health Outcomes Studied:</th>
<th>Drugs Studied:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung function</td>
<td>Inhaled Corticosteroids (ICS)</td>
</tr>
<tr>
<td>Asthma exacerbations requiring systemic steroids</td>
<td>Beclomethasone</td>
</tr>
<tr>
<td>All-cause and asthma specific deaths</td>
<td>Budesonide</td>
</tr>
<tr>
<td>Asthma control composite scores</td>
<td>Ciclesonide</td>
</tr>
<tr>
<td>Asthma-specific quality of life (QOL)</td>
<td>Fluticasone</td>
</tr>
<tr>
<td>Asthma-specific healthcare utilization</td>
<td>Flunisolide</td>
</tr>
</tbody>
</table>

Drugs Studied:

- Beclomethasone
- Budesonide
- Ciclesonide
- Fluticasone
- Flunisolide
- Fluticasone furoate
- Formoterol
- Fumarate dihydrate
- Mometasone
- Olodaterol
- Salmeterol
- Triamcinolone (off market)
- Vilanterol
- Formoterol fumarate dihydrate HFA
- Mometasone furoate + Fluticasone furoate dissociable DPI
- Fluticasone propionate + Salmeterol DPI
- Fluticasone propionate + salmeterol HFA
- Budesonide + formoterol dihydrate HFA

Intermittent inhaled corticosteroids

Health Outcomes Studied:

- Lung function
- Asthma exacerbations requiring systemic steroids
- All-cause and asthma specific deaths
- Asthma control composite scores
- Asthma-specific quality of life (QOL)
- Asthma-specific healthcare utilization

Single Maintenance And Reliever Therapy (SMART)

- Meta-analysis of 16 randomized clinical trials
  - N= 22,524 patients 12 years of age and older
  - N= 341 patients 4-11 years of age
  - 14 RCTs evaluated ICS alone as the controller
  - All RCTs included SABA as a relief therapy for patients 5 years of age and older
  - 15 studies were SMART with budesonide & formoterol dry powder inhaler


0-4 years of age

<table>
<thead>
<tr>
<th>Study Intervention</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermittent ICS + PRN SABA compared to PRN SABA</td>
<td>↓ Risk of systemic corticosteroid need with asthma exacerbation improved QOL</td>
</tr>
<tr>
<td>Intermittent ICS compared to ICS controller</td>
<td>No effect seen on: Use of rescue medications or other measures</td>
</tr>
<tr>
<td>Intermittent ICS compared to no therapy</td>
<td>Insufficient data</td>
</tr>
<tr>
<td>Intermittent ICS compared to non-medication treatment</td>
<td>Insufficient data</td>
</tr>
</tbody>
</table>

12 years and older with persistent asthma

<table>
<thead>
<tr>
<th>Study Intervention</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermittent ICS controller compared to ICS controller</td>
<td>↓ Risk of exacerbation (composite outcome)</td>
</tr>
<tr>
<td>Intermittent ICS compared to ICS controller</td>
<td>Does not effect: QOL, Rescue medication use, Insufficient measures for other outcomes</td>
</tr>
<tr>
<td>ICS/LABA as controller and quick relief compared to a higher ICS dose</td>
<td>↓ Risk of exacerbation (composite outcome)</td>
</tr>
<tr>
<td>ICS/LABA as controller and quick relief compared to ICS/LABA controller at the same ICS dose</td>
<td>↓ Risk of exacerbation (composite outcome)</td>
</tr>
</tbody>
</table>
SMART vs ICS alone as controller
• SMART was associated with:
  ▪ Increased FEV1
  ▪ Decreased need for rescue medication
  ▪ Ages 4-11 years associated with:
  ▪ reduced risk for exacerbation

SMART compared to ICS (with or without LABA) & PRN SABA is associated with lower risk of asthma exacerbation.

SMART vs ICS/LABA as controller
• SMART was associated with decreased risk of:
  ▪ Exacerbation requiring systemic steroid
  ▪ ED visits
  ▪ Hospitalization
• No specific associations with:
  ▪ Mild exacerbations
  ▪ FEV1
  ▪ Asthma Quality of life
  ▪ Lower use of rescue medication inhalations/day

Long-acting muscarinic antagonist for asthma

Long-acting muscarinic antagonist (LAMA)
• LAMAs work on the airway smooth muscle
  ▪ Anticholinergic that blocks acetylcholine, a neurotransmitter
  ▪ Inhibits bronchoconstriction

Addition of LAMA: ≥ 12 years with uncontrolled, persistent asthma
Sobieraj et al. 2018

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICS + LAMA compared to placebo</td>
<td>↓ Risk of systemic corticosteroid need with asthma exacerbation (47%)</td>
</tr>
<tr>
<td>ICS + LAMA compared to doubled ICS dose</td>
<td>No effect found on: Risk of systemic corticosteroid need with asthma exacerbation, spirometry, AQOL, or use of rescue medications</td>
</tr>
<tr>
<td>ICS + LABA compared to ICS + LAMA</td>
<td>No effect found on: Risk of systemic corticosteroid need with asthma exacerbation, asthma related deaths, spirometry, AQOL, ACQ, or use of rescue medications</td>
</tr>
<tr>
<td>ICS/LABA + LAMA compared to ICS + LABA</td>
<td>Improved spirometry (FEV1)</td>
</tr>
</tbody>
</table>

Conclusions: LAMA and intermittent ICS for asthma
• Inhaled SABA has been the preferred reliever of choice for 50 years
• Newer evidence for intermittent ICS use shows:
  ▪ Children ≤ 5 years old with recurrent wheezing
  ▪ Intermittent ICS during an URI decreases asthma exacerbations
  ▪ Patients ≥ 12 years with persistent asthma
  ▪ Intermittent ICS use may be as effective as using them as a controller medication
• Interim inhaled LABA as controller and quick relief therapy reduces asthma exacerbations compared:
  ▪ ICS inhaled alone as a controller
  ▪ ICS/LABA as a controller
• Evidence for patients ≥ 12 years with uncontrolled persistent asthma in adding LAMA to:
  ▪ ICS decreases exacerbations and improves lung function
  ▪ ICS/LABA improves asthma control and lung function
• Cost considerations were not part of studies on new strategies for asthma control

Asthma Clinical Guidelines
### Clinical Guidelines

**Purpose:**
- Provide recommendations to optimize patient care
- Based on systematic review of evidence
- A tool to assist a clinician in medical decision making
- Should not be used to replace clinical judgment

**Asthma Clinical Guidelines:**
- National Asthma Education and Prevention Program EPR 3, 2007 (2020 EPR 4 draft was open for comments January 2020)
- Global Initiative for Asthma 2019
- European Respiratory Society/American Thoracic Society 2019: Guideline Management of Severe Asthma

<table>
<thead>
<tr>
<th>Current Evidence</th>
<th>GINA 2019</th>
<th>NAEP 2007</th>
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<tbody>
<tr>
<td><strong>Preferred Controller</strong></td>
<td>0-4 yrs: Daily low-dose ICS</td>
<td>0 yrs: Daily low-dose ICS</td>
</tr>
<tr>
<td>5-11 yrs: Daily low-dose ICS</td>
<td>5-11 yrs: Medium-dose ICS</td>
<td></td>
</tr>
<tr>
<td>12 yrs: Daily medium-dose ICS or medium-dose LABA and/or SABA</td>
<td>12 yrs: Medium-dose ICS or low-dose OCS</td>
<td></td>
</tr>
</tbody>
</table>

| **Alternative Controller** | 0-4 yrs: Medium-dose ICS + LABA | 0 yrs: Medium-dose ICS |
| 5-11 yrs: Daily medium-dose ICS + LABA and/or SABA | 5-11 yrs: Daily high-dose ICS + LABA or LTRA |
| 12 yrs: Daily medium-dose ICS + LABA and/or SABA | 12 yrs: High-dose ICS + LABA and/or SABA |

| **Reliever** | 0-5 yrs: PRN SABA | 0 yrs: Low-dose ICS/Leukotriene modifiers |
| 6 yrs: Depends on controller | All ages: Low-dose ICS/Leukotriene modifiers |

**STEP 1**

**STEP 2**

**STEP 3**

**STEP 4**

**STEP 5**
Summary of major changes to GINA 2019

- Includes off-label use of PRN ICS/formoterol or ICS taken whenever SABA is taken
- No longer recommends SABA only treatment for ages ≥ 12 years
- Preferred controller for adults and adolescents for Step 1 & Step 2 is low dose ICS/formoterol
- Tiotropium as add-on therapy for ages 6 years and older, preferred over biologics because of cost
- Off-label use of add on low dose azithromycin as an option for symptomatic asthma despite moderate to high-dose ICS-LABA

Potential changes to NAEPP guidelines may include

- Ages 0-4 years: Short course of ICS with PRN SABA with respiratory illness (off-label)
- Over 4 years of age: No use of short term increased ICS dose with illness
- Ages 12 years and older: Use of PRN ICS plus SABA for mild persistent asthma (off-label)
- Ages ≥ 4 years of age with moderate to severe asthma: Use of ICS/formoterol as daily controller and quick relief therapy (off-label)
- Addition of LAMA to ICS or ICS/LABA for poorly controlled asthma

European Respiratory Society and American Thoracic Society (ERS/ATS) Task Force recommendations for severe asthma in adults

- Severe uncontrolled adult eosinophilic asthma phenotypes options: anti-interleukin (IL)-5 (mepolizumab, reslizumab) and anti-IL-5 receptor α (benralizumab)
- Adult patients with severe asthma: Use a blood eosinophil count ≥150 μL⁻¹ to guide anti-IL-5 initiation
- Adolescents or adults with most likely response to anti-IgE therapy (omalizumab): eosinophil ≥250 μL⁻¹ and FeNO ≥19.5 ppb
- Adults with severe eosinophilic asthma and those with severe corticosteroid-dependent asthma (regardless of blood eosinophil levels): anti-IL-4/13 (Dupilumab)
- Adolescents and adults with severe uncontrolled asthma despite GINA step 4–5 or NAEPP step 5 therapies: Add-on tiotropium
- Persistently symptomatic or uncontrolled patients on GINA step 5 or NAEPP step 5 therapies (regardless of asthma phenotype): Trial of chronic macrolide therapy

Considerations

- Cost
  - SABA vs. ICS/LABA
  - ICS + LAMA vs. ICS/LABA
- Insurance drug formulary
- Pharmacy availability
- Safety of prn ICS/formoterol
- Safety of prn SABA
- Antibiotic stewardship

Case studies
Inhaler technique

- Up to 80% of patients use inhalers incorrectly
- Choose appropriate device for age and ability
- Check technique as part of every asthma visit
- Correct technique using teach back (physical demonstration)
- Confirm you can demonstrate correct technique on every device you prescribe and have a checklist of technique available

RediHaler

- Do not shake RediHaler. Do not use with a spacer device.
- Open the white cap. Do not occlude vents on top of inhaler.
- Breathe out fully. Never exhale into the inhaler mouthpiece.
- Place the mouthpiece in your mouth and close your lips around it to form a tight seal.
- Inhale deeply to release the medication. Hold the inhaler upright as you take your inhalations. You will hear a faint clicking noise at the start of inhalation.
- Remove inhaler; hold breath for 5 to 10 seconds.
- Breathe out slowly, away from the inhaler.
- Close the white cap.
- If you take more than one inhalation, close the cap and repeat. Rinse mouth.

Pressurized MDI

- Sub-optimal technique: patients may incorrectly stop inhalation at actuation-50-80% of the medication will be deposited in the oropharynx.
- Overall, inhaled corticosteroid delivery varies from 5-50%.
- Use of a holding chamber recommended
- Optimal technique: Actuation during a slow (30 L/min or 3-5 seconds) deep inhalation followed by 10 second breath hold.

Holding chamber

- Optimal: Rapid (60 L/min or 1-2 seconds) deep inhalation, followed by 10-second breath hold immediately following actuation
- Advantages:
  - No chamber
- Disadvantage:
  - Delivery may be greater or lesser than MDI depending on device and technique

Younger children may not generate sufficient inspiratory flow to activate the inhaler.
- Dose is lost if patient exhales through the device after actuating.

Dry powder inhalers
Diskus
- Do not shake.
- Hold in left hand and place the thumb of right hand in the thumb grip.
- Push the thumb grip away from you as far as it will go until the mouthpiece shows and snaps into place.
- Hold the diskus level, like a "hamburger".
- Slide the lever until it clicks. Do not tilt the diskus.
- Hold breath for 10 seconds or as long as comfortable.
- Place thumb in the thumb grip and slide it back towards you as far as it will go. Make sure the Diskus clicks shut.
- Rinse your mouth.
- Repeat.

RespiClick
- Hold the inhaler with the mouthpiece downward and the top of the inhaler pointing upward.
- Pull the cap down until you hear a click. This loads your medicine dose.
- Breathe out fully, away from the mouthpiece.
- Place the mouthpiece into your mouth with your lips sealed tightly around it. Do not cover the vent with your fingers.
- Breathe in deeply as this will deliver the medicine.
- Take the inhaler out of your mouth and hold for 5 seconds or as long as comfortable.
- Breathe out, away from the mouthpiece.
- If you need another dose, close the cap all the way and repeat steps.

Ellipta
- Do not shake Ellipta.
- Slide the cover down until a click is heard.
- Breathe out gently away from inhaler.
- Put the mouthpiece in mouth and close lips to form a good seal. Do not block air vent with fingers. Breathe in steadily and deeply. Hold your breath for 5 seconds or as long as comfortable.
- Remove inhaler from mouth while holding breath.
- Breathe out gently, away from inhaler.
- Slide the cover upwards as far as it will go, to cover the mouthpiece.
- Rinse your mouth after taking in the medicine.

Twisthaler
- Hold the inhaler straight up with the colored portion on the bottom.
- Hold the colored portion, twist the cap in a counterclockwise direction to remove it. This loads your dose automatically when you remove the cap.
- Turn your head away from the inhaler and exhale fully.
- Put the mouthpiece in your mouth with your lips forming a tight seal.
- Breathe in steadily and deeply as you can.
- Remove the inhaler from your mouth while holding your breath for 5-10 seconds.
- Do not breathe out into the inhaler.
- Replace the cap all the way.
- If you take two puffs, wait 30 seconds and repeat steps.
- Rinse your mouth.