A Breath of Fresh Air?
An update of novel inhalers used for the treatment of asthma and COPD

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RIPF Kimberly McDonough Spring Seminar
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Disclosure

- I have no actual or potential conflicts of interest associated with this presentation or products mentioned within.
Objectives

Pharmacists
- Review indications and dosing for new inhalers in the treatment of asthma/COPD based on current primary literature
- Identify patient specific factors which contribute to non-adherence with current inhaler devices
- Design a therapeutic treatment regimen for patients at high-risk of non-adherence
- Demonstrate proper use of inhaler devices and counseling techniques

Technicians
- Identify patient specific factors which contribute to non-adherence with current inhaler devices
- Review common side effects associated with various inhalers
Evolution of Inhalers
### Table 1: Some FDA-Approved Drugs for COPD

<table>
<thead>
<tr>
<th>Drug</th>
<th>Some Formulations</th>
<th>Delivery Device</th>
<th>Usual Adult Dosage</th>
<th>Cost[^1]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhaled Short-Acting Anticholinergic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipratropium</td>
<td>17 mcg/inhalation</td>
<td>HFA MDI</td>
<td>2 inhalations qid PRN</td>
<td>$215.00</td>
</tr>
<tr>
<td>generic – single-dose vials</td>
<td>200 mcg/ml sol</td>
<td>Nebulizer</td>
<td>500 mcg qid PRN</td>
<td>18.00</td>
</tr>
<tr>
<td>Inhaled Short-Acting Beta-2-Agonist/Short-Acting Anticholinergic Combination</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuterol (Combination)</td>
<td>90 mcg/18 mcg/1800 mcg</td>
<td>CFC MDI</td>
<td>2 inhalations qid PRN</td>
<td>216.00</td>
</tr>
<tr>
<td>Albuterol (Combination)</td>
<td>100 mcg/200 mcg/2000 mcg</td>
<td>MDI</td>
<td>1 inhalation qid PRN</td>
<td>240.00</td>
</tr>
<tr>
<td>Durisol (Combination)</td>
<td>2.5 mg/0.5 mg/75 ml</td>
<td>Nebulizer</td>
<td>2.5 mg/0.5 mg qid PRN</td>
<td>230.00</td>
</tr>
<tr>
<td>Inhaled Long-Acting Beta-2-Agonists</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indacaterol (Combination)</td>
<td>75 mcg/capsule</td>
<td>DPI (30 inhal)</td>
<td>75 mcg once/day</td>
<td>173.00</td>
</tr>
<tr>
<td>Indacaterol (Combination)</td>
<td>50 mcg/bottle</td>
<td>DPI (60 inhal)</td>
<td>50 mcg bid</td>
<td>100.00</td>
</tr>
<tr>
<td>Indacaterol (Combination)</td>
<td>12 mcg/bottle</td>
<td>DPI (12 inhal)</td>
<td>12 mcg bid</td>
<td>183.00</td>
</tr>
<tr>
<td>Indacaterol (Combination)</td>
<td>20 mcg/2 ml/25 mg/ml</td>
<td>Nebulizer</td>
<td>20 mcg bid</td>
<td>472.00</td>
</tr>
<tr>
<td>Indacaterol (Combination)</td>
<td>15 mcg/10 ml/22.5 mg/ml</td>
<td>Nebulizer</td>
<td>15 mcg bid</td>
<td>457.00</td>
</tr>
<tr>
<td>Inhaled Corticosteroids</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluticasone propionate/salmeterol</td>
<td>100, 200, 500 mcg</td>
<td>DPI (60 inhal)</td>
<td>250/50 mcg bid</td>
<td>258.00</td>
</tr>
<tr>
<td>Fluticasone furoate/salmeterol</td>
<td>100, 200, 500 mcg</td>
<td>DPI (60 inhal)</td>
<td>250/50 mcg bid</td>
<td>258.00</td>
</tr>
<tr>
<td>Beclomethasone/budesonide/formoterol/Symbicort[^2]</td>
<td>80, 160 mcg</td>
<td>MDI (120 inhal)</td>
<td>3200 mcg bid</td>
<td>236.00</td>
</tr>
<tr>
<td>Phosphodiesterase-4 Inhibitor</td>
<td>500 mg oral tablets</td>
<td>DPI (500 inhal)</td>
<td>none qid PRN</td>
<td>198.00</td>
</tr>
</tbody>
</table>

[^1]: Cost for 14 days.

### Table 2: Some FDA-Approved Drugs for Asthma

<table>
<thead>
<tr>
<th>Drug</th>
<th>Some Available Formulations</th>
<th>Adult Dosage</th>
<th>Pediatric Dosage</th>
<th>Cost[^1]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhaled Beta-2-Agonists, Short-Acting</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuterol – ProAir HFA (Teva)</td>
<td>HFA MDI (60 or 200 inhal)</td>
<td>90 mcg inhalation</td>
<td>2-4 yrs: 90-180 mcg q4h PRN</td>
<td>$45.00</td>
</tr>
<tr>
<td>generic – single-dose vials</td>
<td>1.63, 2.5 mg/mL</td>
<td>1-2 mg/mL</td>
<td>2-4 yrs: 0.63-2.5 mg q4h PRN</td>
<td>24.00</td>
</tr>
<tr>
<td>Inhaled Corticosteroids</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Budesonide – Pulmicort Flexhaler (AstraZeneca)</td>
<td>DPI (60, 120 inhal)</td>
<td>180-320 mcg bid</td>
<td>2-4 yrs: 40-80 mg q4h PRN</td>
<td>120.00</td>
</tr>
<tr>
<td>generic – single-dose vials</td>
<td>0.25, 0.5 mg/mL</td>
<td>0.5 mg/mL</td>
<td>2-4 yrs: 0.25 mg or 0.5 mg once/day</td>
<td>306.00</td>
</tr>
<tr>
<td>Fluticasone – Flonext (GSK)</td>
<td>HFA MDI (60, 120 inhal)</td>
<td>90-160 mcg bid</td>
<td>2-4 yrs: 90-320 mcg bid</td>
<td>174.00</td>
</tr>
<tr>
<td>generic – single-dose vials</td>
<td>0.25, 0.5 mg/mL</td>
<td>0.5 mg/mL</td>
<td>2-4 yrs: 0.25 mg or 0.5 mg once/day</td>
<td>220.00</td>
</tr>
<tr>
<td>Fluticasone – Flonext (GSK)</td>
<td>HFA MDI (60, 120 inhal)</td>
<td>90-160 mcg bid</td>
<td>2-4 yrs: 90-320 mcg bid</td>
<td>174.00</td>
</tr>
</tbody>
</table>

[^1]: Cost for 14 days.

[^2]: All dosages are for adults. For children under 12 years of age, please see package insert for specific dosing instructions.
Right now you may be thinking...

WAIT

I'M CONFUSED
Or...

"I just want it to stop."
Or maybe…

LETS RUN AWAY TOGETHER

JUST KIDDING I HAVE ASTHMA
Happy Cinco de Mayo!

When she say you're not the Juan.

Que?
Let’s clarify these new devices!
New Inhalers Approved

Since July 2012, the FDA has approved 11 new inhalers/ or devices!

4 Ellipta
4 Respimats
1 Respliclick
1 HFA
1 Pressair
2012
• Turdoza® Pressiar® (7/23/12)
• Anoro™ Ellipta® (12/18/13)

2013

2014
• Asmanex® HFA (4/25/14)
• Striverdi® Respimat (7/31/14)
• Arnuity™ Ellipta® (8/20/14)
• Incruse™ Ellipta® (8/30/14)
• Spiriva® Respimat 2.5 mcg COPD (9/25/14)

2015
• Proair® Respiclick (4/1/15)
• Breo® Ellipta® (4/30/15)
• Stiolto® Respimat (5/26/15)
• Spiriva® Respimat 1.25 mcg Asthma (9/15/15)
Inhalers by device/delivery system

**Dry Powder (DPI)**
- Ellipta
  - Anoro
  - Arnuity
  - Breo
  - Incruse
- Pressair
  - Turdoza
- Respiclick
  - Proair

**HFA**
- Asmanex

**Respimat**
- Spiriva
- Stiolto
- Striverdi
Inhalers by Medication Class

Single
- LABA - Striverdi
- LAMA - Incruse, Spiriva
- ICS - Arnuity
- SABA - Proair, Respiclick

Combination
- LABA/LAMA - Anoro, Stiolto
- LABA/ICS - Breo
Hands on activity!!

PLEASE MAKE GROUPS OF 4 AS WE WILL REVIEW THE NEW DEVICES!!
Ellipta Devices

- Anoro
- Arnuity
- Breo
- Incruse
Ellipta Devices

Storage:
- Must be thrown out once the dose reader reaches zero (at this point, no medicine is left) or 6 weeks after removing from foil pouch, whichever comes first.

Maintenance
- Wipe mouthpiece with dry cloth or cotton swab as needed.
- Do not try to disassemble inhaler or immerse in water.

Precautions
- Patients with severe milk-protein allergies should not use these devices as they may cause severe hypersensitivity reactions.
Ellipta Devices

Administation
- Open the inhaler cover by pushing mouthpiece back.
- Once you hear a click, the mouthpiece is fully exposed.
- Take a deep breath in and breathe out fully and completely, away from the inhaler.
- Place the inhaler to your lips and form a tight seal around the mouthpiece. Take a deep, quick breath in.
- Make sure you do not block the air vent with your fingers.
- Hold your breath for up to 10 seconds, or however long is comfortable.
- Remove the inhaler from your mouth and breathe out.
- Close the inhaler by placing the mouthpiece cover back over the mouthpiece.

Dose counter
- The Ellipta has a dose counter to indicate the number of doses left. When the dose counter turns red, it means you have limited medicine left (<10 doses) and you need a refill.
Anoro
(umeclidinium/vilanterol)

- **Umeclidinium/vilanterol (LAMA + LABA)** combination is indicated for the long-term, once-daily, maintenance treatment of airflow obstruction in patients with COPD, available for delivery via the Ellipta® device.

- **Dosing**
  - 62.5 mcg/25 mcg – 1 puff inhaled by mouth ONCE daily
Anoro
(umeclidinium/vilanterol)

- Clinical trials involving umeclidinium/vilanterol were able to demonstrate significant improvement in pulmonary function and symptom reduction compared to placebo. Additionally, combination therapy of umeclidinium/vilanterol was significantly more effective than once-daily tiotropium, umeclidinium, and vilanterol monotherapies in lung function improvement.

- The German Institute for Quality and Efficiency in Health Care found that combination umeclidinium/vilanterol was not shown to demonstrate benefit over tiotropium.

  - More specifically, in patients with moderate COPD and fewer than two exacerbations per year, umeclidinium/vilanterol did not show any differences in dyspnea and health-related quality of life compared to tiotropium.
Arnuity  
(fluticasone furoate)

- Fluticasone furoate (ICS) is indicated for maintenance treatment of patients with asthma age 12 years and older, available for delivery via the Ellipta® device.
- It is not indicated for acute bronchospasm.
- Dosing
  - 100 or 200 mcg inhaled by mouth once daily
  - Dose based on prior inhaled corticosteroid dose/use
  - Starting dose is 100 mcg inhaled by mouth once daily for mild-moderate persistent asthma
Breo 
(fluticasone/vilanterol)

- Combination fluticasone/vilanterol (ICS + LABA) is indicated for the long-term, once-daily maintenance treatment of airflow obstruction in patients with COPD and asthma (18 years of age or older)
- Fluticasone/vilanterol is also indicated to reduce exacerbations of COPD in patients with a history of exacerbations.

- Fluticasone/vilanterol is the first FDA-approved combination ICS/LABA to offer once-daily dosing for COPD. Currently, there are no head-to-head trials that have demonstrated superiority in the safety or efficacy of fluticasone compared to other ICS

- Dosing
  - Asthma – 100/25 mcg or 200/25 mcg 1 puff inhaled by mouth once daily
  - COPD – 100/25 mcg 1 puff inhaled by mouth once daily
One study found fluticasone/vilanterol significantly improved pulmonary function compared to placebo and fluticasone furoate monotherapy. Additionally, fluticasone/vilanterol demonstrated improved exacerbation rates compared to vilanterol monotherapy.

Onset of action
- Vilanterol also has a quicker onset of action compared to salmeterol.

Despite the novel once-daily offering, the benefits of fluticasone/vilanterol over other twice-daily ICS/LABA combinations are still unclear.

Comparison of fluticasone/vilanterol to vilanterol monotherapy in the reduction of exacerbation rates is difficult to discern, since vilanterol is not available as a monotherapy, and the same was not demonstrated for fluticasone monotherapy.

More meaningful results would be obtained from a direct comparison of fluticasone/vilanterol to fluticasone/salmeterol (ie. Advair)
**Incruse**  
(umeclidinium)

- **Umeclidinium** is a long-acting muscarinic antagonist (LAMA) approved for long-term maintenance of lung function in patients with COPD.

- Umeclidinium is indicated for once daily maintenance of COPD and received its indication based on clinical trials demonstrating improvements in FEV1 and FEV1/FVC in patients:
  - >40 years of age, currently smoking or with at least a 10-year pack history, a post-bronchodilator FEV1 <70% of expected, and a FEV1/FVC <70%

- **Dosing**
  - 62.5 mcg – 1 puff inhaled by mouth once daily
Study results included one randomized placebo-controlled, double-blind, parallel group trial, time to rehospitalization and next COPD exacerbation were delayed by approximately 100 days with umeclidinium compared to placebo.

Significant differences in time to COPD exacerbation, and time to rehospitalization were not observed between umeclidinium and the combination of umeclidinium and vilanterol.
Respimat Devices

Soft Mist

- Spiriva
  - 1.25 mcg – Asthma
  - 2.5 mcg – COPD
- Stiolto
- Striverdi
Respimat

Administration

- Priming required!!
  - Point the inhaler towards the ground (away from your face) and press on the dose-release button until you see a spray.
  - Repeat 3 more times for a total of 4 sprays towards the ground. Your inhaler is ready to use.

- When you haven’t used in more than 3 days, release 1 test spray towards the ground before using.

- When you haven’t If not used within 21 days, release 4 test sprays towards the ground before using.
Administration (cont.)

- Press the small, grey safety catch button on the side and remove the clear base.
- Write the discard date on the cartridge (3 months from 1st date of use).
- Place the cartridge into the inhaler device and press into place until snug. Part of the cartridge (roughly 1/8 inch) will be visible at the bottom of the inhaler. This is normal.
- Place the clear base back on the inhaler.
- Holding the inhaler vertically as shown, twist the clear base in the direction of the white arrows until you hear a click. This will be approximately a half of a turn.
- Flip the blue cap open.
- Take a deep breath and exhale fully away from the inhaler. Place the inhaler to your mouth and form a seal around the mouthpiece with your lips. Be careful not to cover the air vents on the sides with your mouth. Take a deep, slow breath in. Remove the inhaler from your mouth and hold your breath for 10 seconds or less, however long is comfortable. Recap the inhaler once complete.

Dose indicator

- Indicator will move into the red zone when there are 7 days left of medication.
Spiriva Respimat
(tiotropium bromide)

- Tiotropium is a LAMA indicated for long-term, once-daily maintenance bronchodilator treatment of airflow obstruction in patients with COPD.
- There are 2 available strengths
  - 1.25 mcg per 2 actuations – Asthma (Blue cap)
  - 2.5 mcg per 2 actuations – COPD (Aqua cap)
**Stiolto Respimat**
(tiotropium/olodatero)

- Tiotropium/olodaterol is a **LAMA/LABA** combination inhaler approved for the long-term maintenance of lung function in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.

- Tiotropium/olodaterol demonstrated improvement in forced expiratory volume (FEV1) and forced vital capacity (FVC) in patients:
  - 40 years of age or older, currently smoking or with at least a 10-year pack history, with moderate to severe COPD defined as a FEV1 of <80% than predicted, and FEV1/FVC of <70%.

- **Dosing**
  - 2.5 mcg/2.5 mcg – 2 puffs inhaled ONCE daily
Stiolto Respimat
(tiotropium/olodatero)

- Placebo-controlled trials remain the majority of the evidence supporting tiotropium/olodaterol with comparisons only available to the individual components of combination.

- Improvements in the primary outcome of exercise capacity by approximately 50 seconds were observed after tiotropium/olodaterol administration when compared to placebo. Improvements of 0.26 L in FEV1 were also observed when compared to placebo, however the long-term benefits of tiotropium/olodaterol are not available.
Olodaterol is a LABA indicated for long-term, once-daily maintenance bronchodilator treatment of airflow obstruction in patients with COPD.

Compared to placebo, olodaterol was shown to improve lung function, as evaluated by FEV1 area under the curve from 0 to 3 hours, and trough FEV1. Olodaterol demonstrated long-term efficacy and safety in patients with moderate to very severe COPD compared to placebo. These patients were allowed to continue their “usual-care” maintenance therapy other than other LABAs, including LAMAs, SAMAs, ICS, and methylxanthines.
Aclidinium bromide is a LAMA indicated for long-term maintenance therapy for COPD-associated bronchospasm.

Aclidinium received FDA approval after studies demonstrated significant improvements in lung function, health status, and nighttime COPD symptom reduction in COPD patients compared to placebo. Patients enrolled in this trial were greater than 40 years of age, current or former smokers with at least a 10 pack-year history with moderate to severe COPD (30% < FEV1 < 80% predicted and post-bronchodilator FEV1/FVC < 70%)

Dosing

- 400 µg TWICE daily
Turdoza Pressair
(acclidinium bromide)

- **Administration**
  - Remove the mouthpiece cap from the inhaler.
  - Press the green button all the way, and then release your finger from the inhaler.
  - When a green bar appears, this means the dose is ready. If it is red, the dose isn't ready quite yet.
  - Take a deep breath and breathe out completely away from inhaler.
  - Place your lips to the inhaler and form a seal around the mouthpiece. Take a deep, quick breath in until you hear a click. Hold your breath for roughly 10 seconds or however long is comfortable. Remove inhaler from your mouth and cover mouthpiece with dust cover.

- **Dose indicator**
  - Indicator will move into the red zone when there are 7 days left of medication.
Patient education is a critical factor in the use and misuse of medication inhalers. Inhalers represent advanced technology that is considered so easy to use that many patients and clinicians do not receive adequate training in their use. Between 28% and 68% of patients do not use metered-dose inhalers or powder inhalers well enough to benefit from the prescribed medication, and 39 – 67% of nurses, doctors, and respiratory therapists are unable to adequately describe or perform critical steps for using inhalers. Of an estimated $25 billion spent for inhalers, annually $5 – 7 billion is wasted because of inhaler misuse. Reimbursement and teaching strategies to improve patient education could substantially reduce these wasted resources.

Respir Care 2005;50(10):1360 - 1374
Treatment Failure

- Cost
- Improper Technique
- Dosing schedule
- Storage
Improper Technique

- [https://www.youtube.com/watch?v=bDHEEV0M62Y](https://www.youtube.com/watch?v=bDHEEV0M62Y)

- Ask your patients
  - Can you show me how you are using the device?
  - Do you use a spacer?
  - Do you know how fast or slow to inhale the device
    - Many demo inhalers now contain an auditory sound when inspiratory rate is appropriate!
  - Do you understand why you are taking this medication
    - (ie. maintenance vs rescue)
Cost continues to remain one of the top reasons for non-adherence and thus may lead to worsening of respiratory status and hospitalization.
Cost

- **Resources available**
  - **Manufacturer**
    - **Vouchers**
      - Allow for 1-time fill for Medicare, uninsured and commercial insured patients
      - Billed as primary insurance ONLY (NOT processed with other insurances)
  - **Coupons**
    - Only can be used as SECONDARY insurance for cash and commercial paying individuals
  - **Patient Assistance Programs (PAP)**
    - Variable by manufacturer
    - Income dependent but patients can appeal due to financial hardship
    - May provide up to 1 year of medication at no charge!
Cost (cont.)

- Medicare/State
  - Medicare Extra Help
    - Many PAP’s require letter of denial from Extra Help to be approved!

- Discount drug programs
  - GoodRx, LowestMeds, NeedyRx, America’s Drug Card, Blink Health, Rx Outreach, AAA (for your car)
  - Through local pharmacy

**See appendix for a comprehensive listing, website URL’s and phone numbers**
Dosing Schedule

- Adherence
  - Ask
    - Is the inhaler’s administration schedule easy for the person to remember?
    - Does the patient take all of their medications once daily? Or multiple times per day?
    - How do you remember to take your medications?
    - Do you often forget to take your medication?
Improper storage may lead to medication degradation, expiration and inadequate response leading to treatment failure

Ask

Where do you store your medication?

Do you keep your medications in an area which is either too hot, cold or humid?

How do you store your medication when traveling or going on a day trip?
Case studies

Let’s get back into groups to review the patient cases together!
Case #1

MS is a 72 y/o F with a past medical history significant for Type 2 DM, HTN, COPD, OSA, hyperlipidemia, Parkinson’s disease and hyperthyroidism. She presents today to review her current inhaled maintenance inhalers. Upon further review she states that “they don’t work”. Below is a list of her current inhalers and how she takes them.

- Spiriva Handihaler
  - 1 capsule once daily
- Albuterol HFA
  - “as needed”
- Foradil Aerolizer
  - 1 capsule twice daily
Case #1

- What questions do you have for her?
- What potential barriers exist?
- Can you recommend alternate therapies?
- Would your recommendation change if she had memory impairment?
Case #2

- JR is a 64 y/o M presenting today for a hospital follow up after a recent COPD exacerbation. Past medical history significant for Type 2 DM with proliferative retinopathy OU, HTN, OA and RA. He reports that he recently started an inhaler about 3 weeks ago and found it difficult to use. He does not remember the names of his inhalers other than albuterol, only that he is instructed to take it once daily.
Case #2

- What questions do you have for her?
- What potential barriers exist?
- Can you recommend alternate therapies?
- Would your recommendation change if he did not have insurance?
- Would your recommendation change if he is turning 65 years old next week?
Questions??

Thank you!!

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