Respiratory Update: A Review of the Latest FDA-Approved Inhalers for COPD and Asthma and How They Fit into the Current Guidelines

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CPE Information and Disclosures
CDR Tana Triepke declares no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this program, including grants, employment, gifts, stock holdings, and honoraria.

CPE Information
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Overview
• Since 2012, the FDA has approved several new inhalers for COPD and Asthma
• The MOA of the new inhalers remains the same as previous treatment options
• Today we are going to explore the new devices and their place in therapy according to the current guidelines

Pharmacist Learning Objectives
• Identify new treatment options for COPD and Asthma and explain their mechanisms of action.
• Design care plans for patients based on their severity of disease and current guidelines for COPD and Asthma.
• Demonstrate and counsel patients on the use of the latest inhalers for COPD and Asthma.
• Describe the advantages and disadvantages that the new inhalers have over the mainstay treatment options on the market for COPD and Asthma.

Technician Learning Objectives
• Identify new treatment options for the management of COPD and Asthma.
• State the different dosage forms available for the latest FDA approved inhalers.
• Describe the advantages and disadvantages that the new inhalers have over the mainstay treatment options on the market for COPD and Asthma.
Self-Assessment Question 1

A 32yo male presents to the asthma clinic for his initial visit. His triggers include: strong odors, exercise, dust, illness, cold air, smoke, and mold. His current medications include fluticasone 220mcg MDI daily and montelukast 10mg qpm. He is having daytime symptoms 1 day per week, nighttime symptoms once per month, some interference with normal activity, and uses his reliever medication 2 days per week. He completed spirometry in which his FEV₁ was 64% of predicted.

Classify this patient's step and create an appropriate treatment plan.

A. Patient is Step 2 and is well controlled. Continue fluticasone and montelukast and follow up in 6 months.
B. Patient is Step 3 and is well controlled. Continue fluticasone and montelukast and follow up in 6 months.
C. Patient is Step 3 and not well controlled. Increase fluticasone to 440mcg daily and continue montelukast. Follow up in 6 weeks.
D. Patient is Step 4 and not well controlled. Change fluticasone to fluticasone/vilanterol 100/25mcg QD and continue montelukast. Follow up in 6 weeks.

Self-Assessment Question 2

A 63yo female presents to the clinic with SOB. History of smoking 1PPD for 45 years. Upon completion of spirometry, her FEV₁/FVC<0.70 FEV₁ = 78% predicted. She was seen 2 months ago for a COPD exacerbation but was not hospitalized. She scored 15 on her COPD assessment test. She currently uses an albuterol MDI.

What recommendation would you make for this patient?

A. Add Theophylline to her regimen
B. Add either olodaterol 2.5mcg, 2 inhalations daily or umeclidinium 62.5mcg, 1 inhalation daily
C. Add fluticasone DPI 200 mcg, 1 inhalation daily
D. Add fluticasone/vilanterol 100/25mcg 1 inhalation daily plus aclidinium 400mcg 1 inhalation BID

Self-Assessment Question 3

A patient has a severe hypersensitivity to milk proteins, which inhaler is not contraindicated?

A. Tiotropium/Olodaterol (Stiolto)
B. Umeclidinium (Incruse)
C. Aclidinium (Tudorza)
D. Fluticasone/Vilanterol (Breo)

Inhalation Devices

- Metered Dose (MDI)
  - HFA
- Dry Powder (DPI)
  - Diskus
  - Flexhaler
  - Ellipta
  - Pressair
- Soft Mist Inhaler (SMI)
  - Respimat
# Pharmacological Categories

- **Bronchodilators**
  - Beta Agonists (SABA or LABA)
  - Anticholinergics (SAMA or LAMA)

- **Glucocorticoids**
  - Corticosteroids (ICS)

# Latest FDA approved inhalers

- Fluticasone (Arnuity Ellipta)
- Fluticasone/Vilanterol (Breo Ellipta)
- Umeclidinium (Incruse Ellipta)
- Umeclidinium/Vilanterol (Anoro Ellipta)
- Aclidinium (Tudorza Pressair)
- Olodaterol (Striverdi Respimat)
- Tiotropium/Olodaterol (Stiolto Respimat)

## Fluticasone Inhalation Powder (Arnuity Ellipta)

- **MOA:** Corticosteroid
  - Anti-inflammatory activity
- **DPI Device**
- **FDA approved indication:** Asthma
- **Dosing:** ≥12 years of age
  - 100 mcg to 200 mcg per day
  - Medium to High dose
- **Pharmacokinetics**
  - Onset of action: 1-2 weeks
  - Absorption: Lungs <1% GI
  - Half-life elimination: 24 hr
  - Time to peak: 0.5-1 hr

## Administration:

- Open and prepare mouth piece
- Slide Cover down to prepare dose
- Exhale fully, deep breath through mouthpiece 3-4 seconds

## Special Instructions:

- Rinse mouth after use
- Discard 6 weeks after opening foil tray or when counter reads 0
- Doses will be lost if cover is opened and closed
- Cleaning is not required

## Adverse Reactions >10%

- CNS: Fatigue, Malaise, Headache
- GI: Oral Candidiasis
- Neuromuscular and skeletal: Arthritis, Musculoskeletal pain
- Respiratory: Sinus Infection, Sinusitis, Upper Respiratory Infection, Throat Irritation, Nasal Congestion, Nasopharyngitis, Rhinitis, Bronchitis

## Special Populations

- Moderate to Severe hepatic disease

## Contraindications

- Hypersensitivity to fluticasone
- Severe hypersensitivity to milk proteins or lactose

## Warnings

- Deterioration of asthma and acute episodes
- Paradoxical bronchospasm
- Close monitoring for glaucoma and cataracts
- Immunosuppression
Fluticasone/Vilanterol Inhalation Powder (Breo Ellipta)

- MOA: Corticosteroid and Long acting beta-agonist
  - Potent anti-inflammatory activity
  - Relaxes bronchial smooth muscle
- DPI Device
- FDA approved indication: COPD and Asthma
- Dosing: ≥18 years of age
  - Asthma: Fluticasone 100mcg/ Vilanterol 25mcg to 200mcg/25mcg daily
  - COPD: Fluticasone 100mcg/ Vilanterol 25mcg daily
  - Medium to High dose steroid

Fluticasone/Vilanterol Inhalation Powder (Breo Ellipta) continued

- Pharmacokinetics Fluticasone
  - Onset of action: 1-2 weeks
  - Absorption: Lungs <1% GI
  - Half-life elimination: 24 hr
  - Time to peak: 0.5-1 hr
- Pharmacokinetics Vilanterol
  - Onset of action: <10 min
  - Absorption: Lungs <2% GI
  - Half-life elimination: 21.3hr COPD, 16hr asthma
  - Time to peak: 10 min

Fluticasone/Vilanterol Inhalation Powder (Breo Ellipta) continued

- Administration:
  - Open and prepare mouth piece
  - Slide Cover down to prepare dose
  - Exhale fully, deep breath through mouthpiece 3-4 seconds
- Special Instructions:
  - Rinse mouth after use
  - Discard 6 weeks after opening foil tray or when counter reads 0
  - Doses will be lost if cover is opened and closed
  - Cleaning is not required

Fluticasone/Vilanterol Inhalation Powder (Breo Ellipta) continued

- Adverse Reactions 1 to 10%
  - CNS: Headache
  - GI: Oral Candidiasis, Diarrhea, upper abdominal pain
  - Neuromuscular and skeletal: Arthralgia, back pain, bone fracture
  - Respiratory: Sinus Infection, Sinusitis, Upper Respiratory Infection, Pneumonia, Oropharyngeal pain, Throat Irritation, Nasal Congestion, Nasopharyngitis, Rhinitis, Bronchitis, Voice disorder
  - Infection: Influenza
  - Cardiovascular: HTN, Peripheral edema, Extrasystoles, Supraventricular Extrasystole, Ventricular premature Contractions

Fluticasone/Vilanterol Inhalation Powder (Breo Ellipta) continued

- Special populations
  - Moderate to Severe hepatic disease
  - Not indicated for children and adolescents
- Contraindications
  - Hypersensitivity to fluticasone or vilanterol
  - Severe hypersensitivity to milk proteins or lactose
- US Boxed Warning
  - LABAs increase risk of asthma-related death
  - Only use when asthma is not adequately controlled on a long-term asthma control medicine.

Fluticasone/Vilanterol Inhalation Powder (Breo Ellipta) continued

- Warnings
  - Deterioration of COPD and asthma and acute episodes
  - Paradoxical bronchospasm
  - Immunosuppression
  - Close monitoring for glaucoma and cataracts
  - Increased risk of pneumonia in COPD patients
  - Caution in patients with cardiovascular disorders
### Umeclidinium Inhalation Powder (Incruse Ellipta)

- **MOA:** Anticholinergic
  - Bronchodilation in bronchial smooth muscle
- **DPI Device**
- **FDA approved indication:** COPD
- **Dosing:** adults
  - 62.5mcg per day, max dose
- **Pharmacokinetics**
  - Absorption: Lungs
  - Half-life elimination: 11 hr
  - Time to peak: 5-15 min

### Administration:
- Open and prepare mouth piece
- Slide Cover down to prepare dose
- Exhale fully, deep breath through mouthpiece 3-4 seconds

### Special Instructions:
- Doses will be lost if cover is opened and closed
- Cleaning is not required

### Adverse Reactions 1 to 10%
- GI: Upper abdominal pain, toothache
- Neuromuscular and skeletal: Arthralgia, Myalgia
- Respiratory: Upper Respiratory Infection, Cough, Nasopharyngitis, Pharyngitis
- Cardiovascular: Tachycardia

### Contraindications
- Hypersensitivity to Umeclidinium
- Severe hypersensitivity to milk proteins or lactose

### Warnings
- Deterioration of COPD and acute episodes
- Paradoxical bronchospasm
- Caution in patients with narrow-angle glaucoma
- Caution in patients with urinary retention

### Umeclidinium/Vilanterol Inhalation Powder (Anoro Ellipta)

- **MOA:** Anticholinergic and Long acting beta₂-agonist
  - Relaxes bronchial smooth muscle
  - Bronchodilation
- **DPI Device**
- **FDA approved indication:** COPD
- **Dosing:** adults
  - Umeclidinium 62.5mcg/ Vilanterol 25mcg per day
  - Max dose

- **Pharmacokinetics Umeclidinium**
  - Absorption: Lungs
  - Half-life elimination: 11 hr
  - Time to peak: 5-15 min

- **Pharmacokinetics Vilanterol**
  - Absorption: Lungs <2% GI
  - Half-life elimination: 21.3hr COPD, 16hr asthma
  - Time to peak: 10 min
**Umeclidinium/Vilanterol inhalation Powder (Anoro Ellipta)**

- **Administration:**
  - Open and prepare mouth piece
  - Slide Cover down to prepare dose
  - Exhale fully, deep breath through mouthpiece 3-4 seconds
- **Special Instructions:**
  - Discard 6 weeks after opening foil tray or when counter reads 0
  - Doses will be lost if cover is opened and closed
  - Cleaning is not required

- **Adverse Reactions 1 to 10%**
  - Cardiovascular: Chest Pain
  - CNS: Headache, Vertigo
  - Endocrine: DM
  - GI: Diarrhea, Abdominal pain, Nausea, Toothache, Constipation
  - Genitourinary: UTI
  - Neuromuscular and skeletal: Limb pain, arthralgia, back pain, muscle spasm
  - Respiratory: Pharyngitis, Cough, Lower respiratory tract infection, Pleuritic chest pain, Sinusitis

- **Contraindications**
  - Hypersensitivity to Umeclidinium or Vilanterol
  - Severe hypersensitivity to milk proteins or lactose

- **US Boxed Warning**
  - LABAs increase risk of asthma-related death
  - Only use when asthma is not adequately controlled on a long-term asthma control medicine.

- **Warnings**
  - Deterioration of COPD and acute episodes
  - Paradoxical bronchospasm
  - Caution in narrow-angle glaucoma
  - Caution in patients with cardiovascular disorders
  - Caution in patients with urinary retention

**Aclidinium Inhalation Powder (Tudorza Pressair)**

- **MOA:** Anticholinergic
  - Bronchodilation
- **DPI Device**
- **FDA approved indication:** COPD
- **Dosing:** adults
  - 400 mcg twice daily
- **Pharmacokinetics**
  - Half-life elimination: 5-8 hrs
  - Time to peak: 10 min

- **Administration:**
  - Squeeze sides of mouthpiece to remove
  - Press green button down which changes control window from red to green
  - Exhale fully, breath in quickly and deeply through mouthpiece until you hear the click and then hold
  - The control window should then turn red

- **Special Instructions:**
  - Store inside sealed pouch
  - Discard after 45 days after opening, 0 counter, or when device locks
Aclidinium Inhalation Powder (Tudorza Pressair) Continued

- Adverse Reactions 1 to 10%:
  - CNS: Headache, Falling
  - GI: Diarrhea, Toothache, Vomiting
  - Respiratory: Nasopharyngitis, Cough, Rhinitis, Sinusitis
- Contraindications
  - Hypersensitivity to Aclidinium
  - Severe hypersensitivity to milk proteins or lactose

Olodaterol Aerosol Solution (Striverdi Respimat)

- MOA: Long acting beta-agonist
  - Bronchodilation by relaxation of airway smooth muscle
- SMI Device
- FDA approved indication: COPD
- Dosing: adults
  - 2.5 mcg/actuation, 2 inhalations daily
- Pharmacokinetics
  - Onset of action: 5 min
  - Duration: 24 hr
  - Half-life elimination: 7.5 hrs
  - Time to peak: 10-20 min

Warnings
- Deterioration of COPD and acute episodes
- Paradoxical bronchospasm
- Caution in patients with narrow-angle glaucoma
- Caution in patients with urinary retention

Administration:
- Prepare for first use
  - Remove clear base and write expiration date on cartridge
  - Insert cartridge until it clicks and replace clear base
  - Turn device until it clicks
  - Open mouthpiece and breath out slowly
  - Press dose release button while breathing in with lips around mouthpiece
  - Hold breath for 10 seconds
**Olodaterol Aerosol Solution (Striverdi Respimat) Continued**

- **Administration:**
  - Prime inhaler prior to use
    - >21 days from use point down and actuate and repeat 3 times
    - >3 days actuate once before use
- **Special Instructions**
  - Discard 3 months after first use or when the locking mechanism is engaged, whichever comes first.

**Olodaterol Aerosol Solution (Striverdi Respimat) Continued**

- **Adverse Reactions 1-11%:**
  - Respiratory: Nasopharyngitis
  - Dermatologic: Skin Rash
  - Genitourinary: UTI
  - Neuromuscular and skeletal: Back pain, Arthralgia
  - Respiratory: Bronchitis

**Olodaterol Aerosol Solution (Striverdi Respimat) Continued**

- **Contraindications**
  - Monotherapy in asthma treatment
- **US Boxed Warning**
  - LABAs increase risk of asthma-related death
  - Safety and efficacy in treatment of asthma not established
- **Warnings**
  - Deterioration of COPD and acute episodes
  - Paradoxical bronchospasm
  - Caution in patients with cardiovascular disorders

**Tiotropium/Olodaterol Aerosol Solution (Stiolto Respimat)**

- **MOA:** Anticholinergic and Long acting beta-agonist
  - Relaxes bronchial smooth muscle
  - Bronchodilation
- **SMI Device**
- **FDA approved indication:** COPD
- **Dosing:** adults
  - Tiotropium 2.5 mcg/Olodaterol 2.5mcg per actuation
  - 2 actuations per day
  - Max dose

**Tiotropium/Olodaterol Aerosol Solution (Stiolto Respimat) Cont.**

- **Pharmacokinetics Tiotropium**
  - Absorption: Lungs
  - Half-life elimination: 25 hr
  - Time to peak: 5-7 min
- **Pharmacokinetics Olodaterol**
  - Onset of action: 5 min
  - Duration: 24 hr
  - Half-life elimination: 7.5 hrs
  - Time to peak: 10-20 min
Tiotropium/Olodaterol Aerosol Solution (Stiolto Respimat) Cont.

• Administration:
  – Prepare for first use
  • Remove clear base and write expiration date on cartridge
  • Insert cartridge until it clicks and replace clear base
  • Turn device until it clicks
  • Open mouthpiece and breath out slowly
  • Press dose release button while breathing in with lips around mouthpiece
  • Hold breath for 10 seconds

Tiotropium/Olodaterol Aerosol Solution (Stiolto Respimat) Cont.

• Administration:
  – Prime inhaler prior to use
  • >21 days from use point down and actuate and repeat 3 times
  • >3 days actuate once before use

Tiotropium/Olodaterol Aerosol Solution (Stiolto Respimat) Cont.

• Special Instructions
  – Discard 3 months after first use or when the locking mechanism is engaged, whichever comes first.

Tiotropium/Olodaterol Aerosol Solution (Stiolto Respimat) Cont.

• Adverse Reactions 1-12%:
  – Respiratory: Nasopharyngitis
  – Neuromuscular and skeletal: Back pain
  – Respiratory: Cough

• Contraindications
  – Hypersensitivity to tiotropium, ipratropium, olodaterol
  – Use in treatment of asthma without a long-term asthma control medication

Tiotropium/Olodaterol Aerosol Solution (Stiolto Respimat) Cont.

• US Boxed Warning
  – LABAs increase risk of asthma-related death

• Warnings
  – Deterioration of COPD and acute episodes
  – Paradoxical bronchospasm
  – Caution in narrow-angle glaucoma
  – Caution in patients with cardiovascular disorders
  – Caution in patients with urinary retention

Advantages of New FDA approved Inhalers

• Once daily dosing (except Aclidinium)
• No propellants
• SMI
  • Improved coordination of actuation and inhalation
  • Aerosol longer spray duration than MDI, ↓ velocity ↓ oropharyngeal deposition
  • No inspiratory force required
• DPI
  • Few steps for use
  • No coordination of inspiration with actuation
  • Combination LABA/LAMA

Disadvantages of New FDA approved Inhalers

• Insurance coverage
  – Prior authorization
• Expiration after use
  – SMI- 3 months
  – DPI- 6 weeks
• SMI
  – Difficulty using with limited dexterity
• DPI
  – Inspiratory flow rate required
Intermittent Persistent Asthma: Daily Medication

- mMRC grade 0-1
- CAT score <10
- FEV\textsubscript{1}\% ≥ 80%
- No exacerbations/year
- No hospitalizations
- No interference with normal activity
- Nighttime awakenings ≤2/month
- SABA use ≤2 days/week

**Recommended Step for Initiating Treatment**: Step 1

- Symptom Control
- Lung Function
- FEV\textsubscript{1}\% ≥ 80%

**Classification of Asthma Control ≥12 years of age**

- Well Controlled
- Not Well Controlled
- Very Poorly Controlled

**Components of Control**

- Symptoms
- Interference with normal activity
- Lung Function

**Classifications**

- 0-1 exacerbation/year
- >2 exacerbations/year
- ≥2 hospitalizations/year

**Recommended Action for Treatment**: Maintain current step (1=check adherence, environmental control, and comorbid conditions)
Key Points

- New inhalation devices available for:
  - Asthma
    - Fluticasone DPI (Arnuity Ellipta)
    - Fluticasone/Vilanterol DPI (BREO Ellipta)
  - COPD
    - Fluticasone/Vilanterol DPI (BREO Ellipta)
    - Umeclidinium DPI (Incruse Ellipta)
    - Umeclidinium/Vilanterol DPI (Anoro Ellipta)
    - Aclidinium DPI (Tudorza Pressair)
    - Olodaterol SMI (Striverdi Respimat)
    - Tiotropium/Olodaterol SMI (Stiolo Respimat)

Key Points

- New inhalation devices pose some advantages and disadvantages
- MOA of new inhalation devices correlate with the COPD and Asthma guidelines

Answer To Self-Assessment Question 1

- A 32yo male presents to the asthma clinic for his initial visit. His triggers include: strong odors, exercise, dust, illness, cold air, smoke, and mold. His current medications include fluticasone 220mcg MDI daily and montelukast 10mg qpm. He is having daytime symptoms 1 day per week, nighttime symptoms once per month, some interference with normal activity, and uses his reliever medication 2 days per week. He completed spirometry in which his FEV₁ was 64% of predicted.

EPR 3 Asthma Guidelines

<table>
<thead>
<tr>
<th>Components of Control</th>
<th>Classification of Asthma Control ≥ 12 years of age</th>
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<tbody>
<tr>
<td>Symptoms</td>
<td>Well Controlled</td>
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<tr>
<td>≤2 days/week</td>
<td>≤2 days/week</td>
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<tr>
<td>Nighttime awakenings</td>
<td>None</td>
</tr>
<tr>
<td>Interference</td>
<td>≤2x/month</td>
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<td>with normal</td>
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<tr>
<td>activity</td>
<td></td>
</tr>
<tr>
<td>SABA use</td>
<td>≤2x/week</td>
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<tr>
<td>FEV₁ or peak flow</td>
<td>&gt;80% predicted/</td>
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<td>personal best</td>
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<tr>
<td>Validated Questionnaires</td>
<td>ATAQ, ACQ, ACT</td>
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</table>

Recommended Action for Treatment

- Maintain current step
- Step up 1 step
- Step up 1-2 steps

EPR 3 Asthma Guidelines

Intermittent Asthma

- Low dose ICS
- LTRA
- Mast cell stabilizer
- Theophylline

Persistent Asthma: Daily Medication

- Step 1
  - Low dose ICS
  - LTRA
  - Mast cell stabilizer
  - Theophylline

- Step 2
  - Med dose ICS
  - LTRA
  - Theophylline
  - Zileuton

- Step 3
  - High dose ICS
  - LABA
  - Oral corticosteroids

- Step 4
  - Step up if needed
  - Check adherence, environmental control, and comorbid conditions

- Step 5
  - Consider Omalizumab for patients who have allergies

- Step 6
  - Assess Control
  - Step down if possible

Classify this patient’s step and create an appropriate treatment plan.

A. Patient is Step 2 and is well controlled. Continue fluticasone and montelukast and follow up in 6 months.
B. Patient is Step 3 and is well controlled. Continue fluticasone and montelukast and follow up in 6 months.
C. Patient is Step 3 and not well controlled. Increase fluticasone to 440mcg daily and continue montelukast. Follow up in 6 weeks.
D. Patient is Step 4 and not well controlled. Change fluticasone to fluticasone/vilanterol 100/25mcg QD and continue montelukast. Follow up in 6 weeks.
Answer To Self-Assessment Question 2

A 63yo female presents to the clinic with SOB. History of smoking of 1PPD for 45 years. Upon completion of spirometry, her FEV₁/FVC<0.70 FEV₁ = 78% predicted. She was seen 2 months ago for a COPD exacerbation but was not hospitalized. She scored 15 on her COPD assessment test. She currently uses an albuterol MDI.

GOLD 2016 COPD Guidelines

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<th>Recommended 1st Choice</th>
<th>Alternative Choice</th>
<th>Other Possible Treatments</th>
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</thead>
<tbody>
<tr>
<td>A</td>
<td>SAMA or SABA pro</td>
<td>LAMA or LABA or SABA and SAMA</td>
<td>Theophylline</td>
</tr>
<tr>
<td>B</td>
<td>LAMA or LABA</td>
<td>LAMA or LABA</td>
<td>SABA and/or SAMA Theophylline</td>
</tr>
<tr>
<td>C</td>
<td>ICS + LABA or LAMA</td>
<td>LAMA and LABA or LAMA and PDE-4 inhibitor or LABA and PDE-4 inhibitor</td>
<td>SABA and/or SAMA Theophylline</td>
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<tr>
<td>D</td>
<td>ICS + LABA or LAMA</td>
<td>ICS + LABA and LAMA or ICS + LABA and PDE-4</td>
<td>Carbocysteine N-acetylcysteine SABA and/or SAMA Theophylline</td>
</tr>
</tbody>
</table>

What recommendation would you make for this patient?

A. Add Theophylline to her regimen
B. Add either olodaterol 2.5mcg, 2 inhalations daily or umeclidinium 62.5mcg, 1 inhalation daily
C. Add fluticasone DPI 200 mcg, 1 inhalation daily
D. Add fluticasone/vilanterol 100/25mcg 1 inhalation daily plus aclidinium 400mcg 1 inhalation BID

Answer to Self-Assessment Question 3

A patient has a severe hypersensitivity to milk proteins, which inhaler is not contraindicated?

A. Tiotropium/Olodaterol (StiOlo)
B. Umeclidinium (Incruse)
C. Aclidinium (Tudorza)
D. Fluticasone/Vilanterol (Breo)
## References