Pharmacist Objectives

- Discuss the new Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines
- Compare and contrast recently approved medications used in the treatment of pulmonary disease
- Compare and contrast recently approved delivery devices used in the treatment pulmonary disease
- Discuss the treatment of patients with Asthma COPD Overlap Syndrome

Technician Objectives

- Recognize recently approved medications used in the treatment of pulmonary disease
- List recently approved delivery devices used in the treatment of pulmonary disease
- Recognize different medications used in the treatment of patients with Asthma COPD Overlap Syndrome

Outline

1. Review GOLD guidelines
2. Introduce new medications and devices used in the treatment of pulmonary disease
3. Introduce asthma COPD overlap syndrome and treatment

GOLD Guidelines

- Launched in 1997 in collaboration with National Heart, Lung, and Blood Institute, National Institutes of Health and World Health Organization
- Frequently updated
- Use as a tool to implement effective management

COPD Diagnosis

- Indicators of COPD
  - Dyspnea
    - Progressive
    - Persistent
    - Worse with exercise
  - Chronic cough
  - Chronic sputum production
  - History of exposure to risk factors
  - Family history of COPD
- Perform spirometry in patients > 40 years with any indicators

COPD Assessment

- Spirometry
  - Forced expiratory volume in one second (FEV₁)
  - Forced vital capacity (FVC)
  - FEV₁:FVC
- Current level of patient’s symptoms
- Exacerbation risk
- Comorbidities

Spirometric Assessment

- Post-bronchodilator FEV₁:FVC < 0.70
- Post-bronchodilator FEV₁ (% predicted) classifies severity of airflow limitation:

<table>
<thead>
<tr>
<th>GOLD Classification</th>
<th>Severity</th>
<th>FEV₁ (% predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD 1</td>
<td>Mild</td>
<td>FEV₁ ≥ 80% predicted</td>
</tr>
<tr>
<td>GOLD 2</td>
<td>Moderate</td>
<td>FEV₁ 50 – 79% predicted</td>
</tr>
<tr>
<td>GOLD 3</td>
<td>Severe</td>
<td>FEV₁ 30 – 49% predicted</td>
</tr>
<tr>
<td>GOLD 4</td>
<td>Very Severe</td>
<td>FEV₁ &lt; 30% predicted</td>
</tr>
</tbody>
</table>

Symptom Assessment

- Current level of patient’s symptoms
  - Well-validated questionnaires
    - COPD Assessment Test (CAT)
    - Modified British Medical Research Council (mMRC) Questionnaire

Exacerbation Risk Assessment

- Exacerbation risk
  - Acute event characterized by worsening of respiratory symptoms beyond normal day-to-day variations and leads to change in medication
  - Best predictor is a history of previous events
Comorbidities

- Routinely assess
- Treat appropriately

COPD Assessment Tool

Case

AZ is a 65-year-old female with COPD and hypertension who complains of shortness of breath when hurrying or walking uphill. She had 2 exacerbations of COPD last year, both were managed in the outpatient setting with steroids and antibiotics. You administered the CAT questionnaire and she scored 11. Her spirometry results from clinic today show a FEV₁ 45% of predicted and a FEV₁/FVC < 70%

What is your assessment of AA's GOLD grade and group?
A. GOLD Grade 2, Group A
B. GOLD Grade 2, Group B
C. GOLD Grade 3, Group C
D. GOLD Grade 3, Group D

Treatment Goals and Principles

Goals
- Relieve symptoms
- Reduce exacerbations
- Prevent disease progression
- Reduce mortality
- Improve health status
- Improve exercise tolerance

Principles
- Treatment often cumulative
- Individuals differ in treatment response

Non-Pharmacologic Therapy

- Smoking cessation
- Oxygen
- Physical activity
- Pulmonary rehabilitation (groups B-D)
  - Exercise, nutrition, education, smoking cessation, behavioral health
- Vaccinations
  - Annual influenza vaccination
  - Pneumococcal vaccination

Pharmacologic Therapy

- Reduces symptoms
- Reduces frequency and severity of exacerbations
- Improves health status
- Improves exercise tolerance
- Does NOT modify long-term decline in lung function
Pharmacologic Treatment Principles

- Inhaled treatment preferred
- Long-acting bronchodilators preferred
  - Long-acting β₂-agonist (LABA)
  - Long-acting muscarinic antagonist (LAMA)
- Consider combination of mechanisms
- Avoid inhaled corticosteroid monotherapy
- Tailor device based on patient characteristics

Preferred Initial Therapy

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Preferred Therapy</th>
<th>Evaluate Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>Inhaled bronchodilator</td>
<td>Try alternative bronchodilator class</td>
</tr>
<tr>
<td>Group B</td>
<td>Inhaled long-acting bronchodilator</td>
<td>Add second long-acting bronchodilator</td>
</tr>
<tr>
<td>Group C</td>
<td>Inhaled LAMA</td>
<td>Add LABA</td>
</tr>
<tr>
<td>Group D</td>
<td>Inhaled LAMA and LABA</td>
<td>Add inhaled corticosteroid (ICS)</td>
</tr>
</tbody>
</table>

Antibiotics for Exacerbations

- Use in exacerbations controversial
- Give if any of the conditions are met
  - Increased dyspnea and increased sputum volume
  - Increased sputum purulence plus increased sputum volume
  - Increased sputum purulence plus increased dyspnea
  - Mechanical ventilation

Recent COPD Drug Approvals

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
<th>Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevespi Aerosphere™</td>
<td>Glycopyrrolate and formoterol</td>
<td>April, 2016</td>
</tr>
<tr>
<td>Seebri™ Neohaler®</td>
<td>Glycopyrrolate</td>
<td>October, 2015</td>
</tr>
<tr>
<td>Utibron™ Neohaler®</td>
<td>Indacaterol and glycopyrrolate</td>
<td>October, 2015</td>
</tr>
</tbody>
</table>

Utibron™ Neohaler®
indacaterol and glycopyrrolate

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Indication</th>
<th>Dosing</th>
<th>Device</th>
<th>Contraindication</th>
</tr>
</thead>
<tbody>
<tr>
<td>LABA/LAMA</td>
<td>Long-term, maintenance treatment of airflow obstruction in patients with COPD</td>
<td>Inhale contents of one capsule (27.5 mcg indacaterol/15.6 mcg glycopyrrolate) twice daily</td>
<td>Dry powder inhaler (DPI)</td>
<td>Box warning for asthma-related deaths</td>
</tr>
<tr>
<td></td>
<td>No adjustment for geriatric patients, mild - moderate renal impairment, or mild - moderate hepatic impairment</td>
<td>No priming, no shaking, contains lactose</td>
<td>Capsules should be stored in the blister and removed immediately before use</td>
<td>Hypersensitivity to indacaterol, glycopyrrolate or any of the ingredients</td>
</tr>
</tbody>
</table>

Utibron™ Neohaler®
Warnings and Precautions

- Asthma-related death
- Deterioration of disease and acute episodes
- Excessive use or use with other LABAs
- Paradoxical bronchospasm
- Immediate hypersensitivity reactions
- Cardiovascular effects
- Use with caution in patients with convulsive disorders, thyrotoxicosis, sensitivity to sympathomimetic drugs, diabetes mellitus, ketoacidosis
- Worsening of narrow-angle glaucoma
- Worsening of urinary retention
- Hypokalemia and hyperglycemia
**Utibron™ Neohaler® Adverse Reactions**

- Adverse reactions (≥ 1% incidence and more common than with placebo)

<table>
<thead>
<tr>
<th>1%</th>
<th>≥ 1% - &lt;5%</th>
<th>5% - &lt;10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharyngitis</td>
<td>Hypertension</td>
<td>Back pain</td>
</tr>
<tr>
<td>Oropharyngeal pain</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Utibron™ Neohaler® Drug Interactions**

- Adrenergic drugs
  - Potentiate effect
- Xanthine derivatives, steroids, diuretics, non-potassium sparing diuretics
  - Potentiate hypokalemia or ECG changes
- Monoamine oxidase inhibitors, tricyclic antidepressants, QTc prolonging drugs
  - Potentiate effect on cardiovascular system
- Beta-blockers
  - Decrease effectiveness, potential bronchospasm
- Anticholinergics
  - Additive effect

**Utibron™ Neohaler® Place in Therapy**

- Improvements in pulmonary function tests and health status

*Am J Resp Crit Care Med 2015;192(9):1068-1079*

<table>
<thead>
<tr>
<th>Patient Category</th>
<th>Utibron™ Neohaler® Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Not initial choice</td>
</tr>
<tr>
<td>B</td>
<td>Not initial choice</td>
</tr>
<tr>
<td>C</td>
<td>Not initial choice</td>
</tr>
<tr>
<td>D</td>
<td>Initial choice</td>
</tr>
</tbody>
</table>

**Seebri™ Neohaler® glycopyrrolate**

- Medication Class: LAMA
- Indication: Long-term, maintenance treatment of airflow obstruction in patients with COPD
- Dosing: Inhalate contents of one capsule (15.6 mcg) twice daily
  - No adjustments for geriatric patients, mild-to-moderate renal impairment, or mild-to-moderate hepatic impairment
- Device: DPI
  - No priming, shaking
  - Contains lactose
  - Capsules should be stored in the blister and removed immediately before use
  - Routine cleaning not required
- Contraindication: History of known hypersensitivity to glycopyrrolate or to any of the ingredients

**Seebri™ Neohaler® Warnings and Precautions**

- Deterioration of disease and acute episodes
- Paradoxical bronchospasm
- Immediate hypersensitivity reaction
- Worsening of narrow-angle glaucoma
- Worsening of urinary retention

**Seebri™ Neohaler® Adverse Reactions and Drug Interactions**

- Adverse reactions (≥ 1% and higher than placebo)

<table>
<thead>
<tr>
<th>≥ 10%</th>
<th>5% - &lt;10%</th>
<th>&lt; 1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper respiratory tract infection</td>
<td>Nasopharyngitis</td>
<td>Sinusitis</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>Oropharyngeal pain</td>
<td></td>
</tr>
</tbody>
</table>

- Drug interactions
  - Anticholinergics
Seebri™ Neohaler®
Place in Therapy

• Improvements in pulmonary function tests and health status

Resp Research 2011;12:156

<table>
<thead>
<tr>
<th>Patient Category</th>
<th>Seebri™ Neohaler® Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Initial choice</td>
</tr>
<tr>
<td>B</td>
<td>Initial choice</td>
</tr>
<tr>
<td>C</td>
<td>Initial choice</td>
</tr>
<tr>
<td>D</td>
<td>First choice in combination with LABA</td>
</tr>
</tbody>
</table>

Using the Neohaler®

1. Don’t swallow the capsules!
2. Pull off cap
3. Open inhaler
4. Prepare capsule, insert capsule into capsule chamber
5. Close the inhaler, hold inhaler upright
6. Pierce the capsule by pressing piercing buttons one time
7. Release piercing buttons fully

Using the Neohaler®

8. Breathe out, don’t breathe into mouthpiece
9. Make sure piercing buttons are to the left and right of inhaler. Put mouthpiece between lips, close lips around mouthpiece
10. Breathe in rapidly but steadily, as deeply as possible through mouth. There will be a whirring noise
11. Remove inhaler from mouth and hold breath for 5-10 seconds or as long as comfortable, breathe out
12. Open inhaler to see if any powder is left in capsule, repeat inhalation if necessary
13. Remove the capsule, close the inhaler, replace cap

Bevespi Aerosphere™
Medication Indication Dosing Device Contraindication

LAMA/LABA
• Long-term, maintenance treatment of airflow obstruction in patients with COPD
• 2 inhalations (2 mg glycopyrrolate and 4.8 mg formoterol) twice daily
• No adjustments for geriatric patients
• Not studied in hepatic impairment, renal impairment [monitor]

MDI
• Priming: 4 sprays
• Repirme: 2 sprays if not used > 7 days and after cleaning
• Expires 3 months after removal from foil pouch
• Dose indicator, display window turns red with 20 puffs remaining
• Clean actuator weekly, run warm water through for 30 seconds, turn and repeat. Let air dry overnight

Box warning for asthma-related deaths
• Hypersensitivity to glycopyrrolate, formoterol fumarate or any component of product

Bevespi Aerosphere™
Warnings and Precautions

• Asthma-related death
• Deterioration of disease and acute episodes
• Excessive use or use with other LABAs
• Paradoxical bronchospasm
• Immediate hypersensitivity reactions
• Cardiovascular effects
• Use with caution in patients with convulsive disorders, thyrotoxicosis, diabetes mellitus, ketoacidosis
• Worsening of narrow-angle glaucoma
• Worsening of urinary retention
• Hypokalemia and hyperglycemia

Bevespi Aerosphere™
Adverse Reactions

• Adverse reactions (≥ 2% incidence and more common than with placebo)

<table>
<thead>
<tr>
<th>1%</th>
<th>&gt; 1% - &lt; 5%</th>
<th>≥ 5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>Urinary tract infections</td>
<td></td>
</tr>
</tbody>
</table>
Bevespi Aerosphere™

Drug Interactions

- Adrenergic drugs
  - Potentiate effect
- Xanthine derivatives, steroids, diuretics, non-potassium sparing diuretics
  - Potentiate hypokalemia or ECG changes
- Monoamine oxidase inhibitors, tricyclic antidepressants, QTc prolonging drugs
  - Potentiate effect on cardiovascular system
- Beta-blockers
  - Decrease effectiveness, potential bronchospasm
- Anticholinergics
  - Additive effect

Bevespi Aerosphere™

Place in Therapy

- Improvements in pulmonary function tests and health status

<table>
<thead>
<tr>
<th>Patient Category</th>
<th>Bevespi Aerosphere™ Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Not initial choice</td>
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<tr>
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<td>Not initial choice</td>
</tr>
<tr>
<td>C</td>
<td>Not initial choice</td>
</tr>
<tr>
<td>D</td>
<td>Initial choice</td>
</tr>
</tbody>
</table>

Recent Asthma Drug Approvals

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
<th>Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qvar® RediHaler™</td>
<td>beclomethasone dipropionate</td>
<td>August, 2017</td>
</tr>
<tr>
<td>ArmonAir™ RespiClick®</td>
<td>fluticasone propionate</td>
<td>January, 2017</td>
</tr>
<tr>
<td>AirDuo™ RespiClick®</td>
<td>fluticasone propionate and salmeterol</td>
<td>January, 2017</td>
</tr>
</tbody>
</table>

Case

Which of the following is the most appropriate recommendation for the initial treatment of AZ’s COPD?
A. Utibron™ Neohaler®
B. Seebri™ Neohaler®
C. Bevespi Aerosphere™
D. Nothing – TK’s COPD is mild and doesn’t require pharmacotherapy

AirDuo™ RespiClick®
fluticasone propionate and salmeterol

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Indication</th>
<th>Dosing</th>
<th>Device</th>
<th>Contraindication</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICS/LABA</td>
<td>Treatment of asthma in patients 12 years and older</td>
<td>1 inhalation (BD 50 mcg/113 mcg, MD 113 mcg/252 mcg) fluticasone propionate/salmeterol</td>
<td>DPI</td>
<td>Box warning for asthma-related deaths</td>
</tr>
<tr>
<td></td>
<td>No overall differences in safety and efficacy in patients ≥ 65 years</td>
<td></td>
<td></td>
<td>Hypersensitivity to milk protein or any ingredients of product</td>
</tr>
<tr>
<td></td>
<td>No formal hepatic impairment studies, monitor patients with hepatic disease</td>
<td></td>
<td></td>
<td>Primary treatment of status asthmaticus or acute episodes of asthma requiring intensive measures</td>
</tr>
<tr>
<td></td>
<td>No formal renal studies</td>
<td></td>
<td></td>
<td>Gently wipe mouthpiece with dry cloth or tissue if needed</td>
</tr>
</tbody>
</table>

AirDuo™ RespiClick®

- Authorized generic launched at same time
  - Not a generic substitute for Advair®
- RespiClick Device
  - Delivery of medication is improved?
  - Lower doses can be administered
**AirDuo™ RespiClick® Dose Ranging Studies**

- Fluticasone propionate
  - 50 mcg from RespiClick® provided similar efficacy as 100 mcg from Diskus®
  - Similar systemic exposure
  
  J Asthma 2017;54(1):89-98

- Salmeterol
  - 12.5 mcg from RespiClick® provided similar efficacy as 50 mcg from Diskus®

  Allergy Asthma Proc 2016;37(4):291-301

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**Fluticasone Dose Response**

![Fluticasone Dose Response Graph]

J Asthma 2017;54(1):89-98

---

**Salmeterol Dose Response**

![Salmeterol Dose Response Graph]

---

**ArmonAir™ RespiClick® fluticasone propionate**

- Treatment of asthma in patients 12 years and older
- No overall differences in safety and efficacy in patients ≥ 65 years
- No formal hepatic impairment studies, monitor patients with hepatic disease
- No formal renal studies
- No formal hepatic impairment studies, monitor patients with hepatic disease
- No formal renal studies
- Hypersensitivity to milk protein or any ingredients of product
- Primary treatment of status asthmaticus or acute episodes of asthma requiring intensive measures

---

**Using the RespiClick®**

1. Hold inhaler upright
2. Open cap back until you hear a “click”
3. Don’t open cap unless you are taking a dose
4. Breathe out through mouth away from inhaler
5. Put mouthpiece into mouth and close lips around
6. Breathe in quickly and deeply through mouth
7. Don’t block the vent
8. Remove inhaler from mouth
9. Hold breath for 10 seconds or as long as comfortable
10. Close cap firmly over mouthpiece

---

**Qvar® RediHaler™ beclomethasone dipropionate**

- Breath-actuated inhaler
  - No need for coordination of actuation with inhalation
  - No shaking, priming, valved holding chamber
  - Routine maintenance not required, gently wipe mouthpiece with dry cloth or tissue
- Available as 40 and 80 mcg/puff
- Available first quarter of 2018
  - Qvar® MDI formulation will be discontinued
How to Use the RediHaler™

1. Open the cap when ready to take dose
2. Breathe out fully away from mouthpiece
3. Place mouthpiece in mouth, close lips around with a good seal
4. Inhale deeply to release the medicine
5. Remove inhaler, hold breath for 5-10 seconds. Breathe out slowly away from inhaler
6. Close the cap after inhaling to prepare for next inhalation

Asthma COPD Overlap Syndrome (ACOS)

- Distinguishing COPD from asthma can be problematic
  - Smokers
  - Older adults
- Diagnostic label, treatment?
  - Minimal research available

Features that Favor Asthma or COPD

<table>
<thead>
<tr>
<th>More likely to be asthma</th>
<th>More likely to be COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Onset before age 20 years</td>
<td>☐ Onset after age 40 years</td>
</tr>
<tr>
<td>☐ Variable in symptoms over minutes, hours or days</td>
<td>☐ Persistent symptoms despite treatment</td>
</tr>
<tr>
<td>☐ Symptoms worse during night or early morning</td>
<td>☐ Always daily symptoms and exertional dyspnea</td>
</tr>
<tr>
<td>☐ Symptoms triggered by exercise, allergens</td>
<td>☐ Chronic cough, sputum preceded onset of dyspnea, unrelated to triggers</td>
</tr>
<tr>
<td>☐ Variable airflow limitation</td>
<td>☐ Persistent airflow limitation; FEV1/FVC &lt;0.7</td>
</tr>
<tr>
<td>☐ Lung function normal between symptoms</td>
<td>☐ Lung function abnormal between symptoms</td>
</tr>
<tr>
<td>☐ Previous diagnosis of asthma</td>
<td>☐ Previous diagnosis of COPD, chronic bronchitis, emphysema</td>
</tr>
<tr>
<td>☐ Family history of asthma, other allergic conditions (allergic rhinitis, eczema)</td>
<td>☐ Heavy exposure to a risk factor</td>
</tr>
<tr>
<td>☐ May improve spontaneously, with bronchodilator or inhaled corticosteroid</td>
<td>☐ Rapid-acting bronchodilator provides limited relief</td>
</tr>
<tr>
<td>☐ Normal chest x-ray</td>
<td>☐ Severe hyperinflation on chest x-ray</td>
</tr>
</tbody>
</table>

ACOS

- Patients with ACOS compared to asthma or COPD alone
  - Frequent exacerbations
  - Poor quality of life
  - High mortality
  - More rapid decline in lung function
  - Consume disproportionate amount of healthcare resources

ACOS

- ≥ 3 boxes checked for either asthma or COPD patient is likely to have that disease
- Similar numbers of checked boxes consider ACOS

Asthma COPD Overlap Syndrome Treatment

- Inhaled corticosteroid
- Add on a LABA and/or LAMA
- Don’t treat with a LABA without an inhaled corticosteroid
<table>
<thead>
<tr>
<th>Pulmonary Update</th>
</tr>
</thead>
<tbody>
<tr>
<td>Questions?</td>
</tr>
</tbody>
</table>