Prescription Updates from the Heart... ...to the Lungs

Objectives

- Understand and classify the medications which were FDA approved within the last four years for Heart Failure, Dyslipidemia, COPD, PAH, as well as Anticoagulants within the last eight years.

- Recognize the clinical nuances of medications which were FDA approved within the last four years for Heart Failure, Dyslipidemia, COPD, PAH, as well as Anticoagulants within the last eight years.

- Recognize the side effects of medications which were FDA approved within the last four years for Heart Failure, Dyslipidemia, COPD, PAH, as well as Anticoagulants within the last eight years.

- When given a patient case, be able to apply the clinical utility of medications which were FDA approved within the last four years for Heart Failure, Dyslipidemia, COPD, PAH, as well as Anticoagulants within the last eight years.

Disclosure

B. Blake Miller has no financial relationships to disclose with regard to this presentation.
Comparison of Anticoagulants

<table>
<thead>
<tr>
<th>Basic Characteristics of Warfarin and DOACs</th>
<th>Warfarin</th>
<th>DOACs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Slow</td>
<td>Rapid</td>
</tr>
<tr>
<td>Dosing</td>
<td>Variable</td>
<td>Fixed</td>
</tr>
<tr>
<td>Food effect</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Medication interactions</td>
<td>Many</td>
<td>Few</td>
</tr>
<tr>
<td>Monitoring Required</td>
<td>Yes (frequent)</td>
<td>Minor</td>
</tr>
</tbody>
</table>

**Pradaxa (dabigatran)**
- direct thrombin inhibitor
- *Thromboembolism (e.g., stroke) prevention in nonvalvular AF*: 150 mg BID
- *DVT/PE treatment (following 5 to 10 days’ treatment with parenteral AC/prevention of recurrence)*: 150 mg BID. (Start 0 to 2 hours before the next dose of parenteral AC would have been due, or at the time of discontinuation of heparin drip.)
- *VTE prevention post-op replacement*: 220 mg once daily for 28 to 35 days. (If started on day of surgery [1 to 4 hrs postop], assume hematostasis achieved; initial dose is 110 mg.)

**Xarelto (rivaroxaban)**
- direct factor Xa inhibitor
- *Thromboembolism (e.g., stroke) prevention in nonvalvular AF*: 20 mg once daily with evening meal to improve absorption
  - *CrCl* ≤ 50 mL/min: 15 mg daily with evening meal
  - *VTE prevention post-op/knee replacement*: 10 mg once daily for 35 days [hip] or 12 days [knee] starting 6 to 10 hrs postop, assuming hematostasis achieved
  - *DVT/PE treatment/prevention of recurrence*: 15 mg twice daily w/o food x 3 weeks, then 20 mg once daily w/o food x 6 months, then 10 mg once daily
- *CV risk reduction in patients with CAD or PAD*: 2.5 mg twice daily, with aspirin 75 to 100 mg once daily

**Eliquis (apixaban)**
- direct factor Xa inhibitor
- *Thromboembolism (e.g., stroke) prevention in nonvalvular AF*: 5 mg BID
  - *2.5 mg BID for patients aged ≥ 80 years, weight ≤ 60 kg, or ≥ 1.5 mg/dL*
  - *VTE prevention post-op/knee replacement*: 2.5 mg twice daily for 35 days [hip] or 12 days [knee] starting 12-24 hrs post-op
  - *DVT/PE treatment*: 10 mg BID x 7 days, then 5 mg BID
  - *DVT/PE prevention of recurrence*: 2.5 mg BID after at least six months of treatment

**Savaysa (edoxaban)**
- direct factor Xa inhibitor
- *Thromboembolism (e.g., stroke) prevention in nonvalvular AF*: 60 mg once daily
  - *CrCl 15 to 50 mL/min: 30 mg once daily*
  - *Not for use in patients with CrCl >95 mL/min*
  - *DVT/PE treatment (following 5 to 10 days’ treatment with a parenteral anticoagulant)*: 60 mg once daily
- *DVT/PE prevention of recurrence*: 30 mg once daily

**Bevyxxa (betrixaban)**
- direct factor Xa inhibitor
- *VTE prevention in acutely ill medical, non-surgical patients with moderate or severely limited mobility plus other VTE risk factors*
  - *160 mg x 1, then 80 mg once daily with food for 35 to 42 days*
  - *Renal dosing*: *CrCl 15 to <30 mL/min: 60 mg x 1, then 40 mg once daily with food x 35-42 days*

**Low molecular weight heparin**
- *Enoxaparin*
- *Dabigatran*
DOACs compared to Warfarin

**PROS**
- Same to lower incidence of safety
- Same to improved incidence of efficacy outcomes
- No INR monitoring
- Bridging therapy likely not needed for most
- Short half-life allows for easier perioperative management
- Fewer drug/diet/co-morbidity interactions
- Less complex patient/family education
- Follow-up can likely be performed by community providers as well as specialty clinics

**CONS**
- DOACs with BID dosing (Pradaxa and Eliquis) and Xarelto’s requirement to take with food may have a negative impact on compliance
- No specific monitoring parameter and not all have perfect reversal agents (expensive)
- Higher incidence of GI side effects and discontinuation rate
- Lack of monitoring may result in non-compliance and an increased chance that patient may not report bleeding
- Renal monitoring and dose adjustment required
- Much higher out-of-pocket costs/copays

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**Stepwise Approach to Anticoagulation in the Prevention of Stroke and Systemic Embolism in Atrial Fibrillation**

**Step 1: Risk Stratification**

<table>
<thead>
<tr>
<th>CHA2DS2-VASc Score</th>
<th>Choice of Whether or Not to Anticoagulate Based on Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHA2DS2-VASc = 0</td>
<td>No anticoagulant necessary</td>
</tr>
<tr>
<td>CHA2DS2-VASc = 1</td>
<td>1 in men and 2 in women: Anticoagulant may be considered</td>
</tr>
<tr>
<td>CHA2DS2-VASc ≥ 2</td>
<td>≥ 2 in men or ≥ 3 in women: Anticoagulant recommended</td>
</tr>
</tbody>
</table>

**Step 2: Choice of Whether or Not to Anticoagulate Based on Score**

<table>
<thead>
<tr>
<th>CHA2DS2-VASc</th>
<th>Choice of Anticoagulant</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No anticoagulant necessary</td>
</tr>
<tr>
<td>1</td>
<td>1 in men and 2 in women: Anticoagulant may be considered</td>
</tr>
<tr>
<td>≥ 2</td>
<td>≥ 2 in men or ≥ 3 in women: Anticoagulant recommended</td>
</tr>
</tbody>
</table>

Notation: DOACs preferred

- **Warfarin**
  - INR 15-50: 30 mg daily (if CrCl > 95, DO NOT USE)
  - Or
    - Xarelto 20 mg with evening meal
      - (if CrCl 15-50: 15 mg daily)
    - Or
      - Savaysa 60 mg daily
    - Or
      - Pradaxa 150 mg BID
        - (if CrCl 15-30: 75 mg BID, avoid if also receiving concomitant P-gp inhibitor)
    - Or
      - Eliquis 5 mg BID
        - (if CrCl 15-30: 75 mg BID, avoid if also receiving concomitant P-gp inhibitor)

Duration of therapy = indefinite (unless patient converted to normal sinus rhythm)
Case #1

CD is a 65 year old female presenting today with newly diagnosed Atrial Fibrillation. She is rate controlled, but needs an anticoagulant recommendation.

Current Medication List:
- Albuterol (SABA) 1 puff every 4-6 hours PRN
- Aspirin 81 mg daily
- Atorvastatin 40 mg each evening
- Lisinopril 5 mg daily
- Metoprolol tartrate 50 mg twice daily
- Stiolto Respimat (Tiotropium + Olodaterol) (LAMA + LABA) 2 inhalations once daily

PMH:
- Atrial Fibrillation
- COPD
- Dyslipidemia
- Hypertension
- History of MI

Vitals from today:
- Height: 65 inches
- Weight: 120 lbs
- Blood Pressure: 135/90
- Heart Rate: 70 bpm
- O2 Saturation: 97%

Labwork from today:
- BUN: 20 mg/dL
- SCr: 1.0 mg/dL
- K+: 4.0 mEq/L
- Glucose: 99 mg/dL
- INR: 1.1
- Hemoglobin / Hematocrit: 16 g/dL / 50%
- Platelets: 400,000 cells/µL

What would you do for CD to reduce her risk of stroke or systemic embolism in Atrial Fibrillation?

A. Increase Metoprolol tartrate to 100 mg BID.
B. Initiate Warfarin 5 mg daily and repeat INR in 2 weeks.
C. Initiate Eliquis 5 mg BID.
D. Initiate Bevyxxa 80 mg once daily with food.
**PCSK9 (Proprotein Convertase Subtilisin-Kexin type-9) Inhibitors**

- Liver-derived protease enzyme
- This enzyme controls the number of low-density lipoprotein receptors
  - PCSK9 mutations reduce receptors in the liver by binding to them to promote degradation
  - This leads to high LDL in blood
  - If you block PCSK9 and there is high LDL in blood, body will make more receptors to get rid of LDL from the blood

---

**2018 ACC/AHA cholesterol guidelines**

- **Primary Prevention**
  - Age 40-75 years
  - LDL-C > 190 mg/dL
  - LDL-C > 160 mg/dL with age ≥ 75 years

- **Secondary Prevention**
  - LDL-C > 130 mg/dL
  - LDL-C > 100 mg/dL with additional risk factors

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**Without PCSK9 Inhibition**

- PCSK9 leads to LDL receptor degradation
- The decrease in LDL receptor number results in higher levels of LDL-C

**With PCSK9 Inhibition**

- PCSK9 inhibition reduces LDL-C levels
- LDL-C receptors are not degraded

---

**In combination with diet AND max tolerated statin in adults with:**

- Heterozygous familial hypercholesterolemia (HeFH) condition that runs in family causing very high LDL
- ASCVD heart problems due to plaque buildup in artery walls
- Uncontrolled LDL when highest tolerated statin not enough to ↓ LDL

---

**To reduce risk of cardiovascular events in patients with CV disease, as adjunct to diet alone or in combination with statins in patients with:**

- Homozygous familial hypercholesterolemia (HoFH)
- ASCVD
- Hyperlipidemia (including HeFH)
### Drug Dosing and Lipid Effects Outcomes Data Comments

<table>
<thead>
<tr>
<th>Drug</th>
<th>Approx Cost for 30-day supply</th>
<th>Dosing and Lipid Effects</th>
<th>Outcomes Data</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Praluent (alirocumab)</td>
<td>US: $1,100</td>
<td>LDL ↓: ~45% to 48% (when added to a statin)</td>
<td>Post-hoc analysis suggests alirocumab in combination with maximally tolerated statin doses may reduce major CV events in high-risk patients.</td>
<td>• Very expensive (~$14,000/yr) - BUT 0$ copay card for commercial insurance worth up to $5,500/yr.</td>
</tr>
<tr>
<td>Repatha (evolocumab)</td>
<td>US: $1,100</td>
<td>LDL ↓: ~42% to 65% (regardless of statin)</td>
<td>• Lowered LDL 34% to 38.5% more compared to ezetimibe. • Added to a high- or moderate-dose statin, prevents 1 CV death, MI, or stroke for every 67 high risk CVD patients treated for about 2 years (FOURIER study). CV death as a standalone outcome not affected.</td>
<td>• Very expensive (~$14,000/yr) - BUT, in alignment with the AHA’s Value in Healthcare Initiative, in Oct’18 Amgen announced that the price of Repatha, will be reduced by 60%, from an annual price of $14,100 down to $5,585. • Consider with other lipid-lowering therapies for HoFH or clinical CVD requiring additional LDL ↓. • Administer via SQ injection. • No long-term safety data. • Potential side effects: running nose, sore throat, cold sx, flu-like sx, back pain, high blood sugar levels, redness, pain, or bruising at injection site.</td>
</tr>
</tbody>
</table>


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### Types of Heart Failure

- **Heart Failure with preserved Ejection Fraction (HFrEF) – EF ≥ 50% (Diastolic HF)**
  - Normal chamber size with normal emptying but impaired filling
  - Result:
    - ↑ Ejection Fraction
    - ↓ left ventricular end diastolic volume
    - ↓ SV and therefore ↓ CO
    - Impairment in ability of heart to fill with blood and relax

- **Heart Failure with reduced Ejection Fraction (HFrEF) – EF ≤ 40% (Systolic HF)**
  - Dilated chamber has reduced wall motion but preserved filling
  - Result:
    - ↓ Ejection Fraction due to ↓ contractility
    - ↑ left ventricular end diastolic volume
    - ↑ SV and therefore ↑ CO
    - Impairment of pumping


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### Imbalance in Neurohormonal Systems drives HF Progression

- **Vasodilation**
  - Natriuresis
  - Diuresis
  - Proangiogenic actions
  - ↓ BP
  - ↑ Sympathetic tone
  - ↑ Aldosterone
  - ↑ Hypertrophy
  - ↑ Fibrosis

- **Vasoconstriction**
  - ↑ Renin (↑ RAAS activity)
  - ↑ HR
  - ↑ Contractility

Survival versus Symptoms

**Mortality benefit**
- Beta Blockers
- ACE-inhibitors/ARBs
- Aldosterone Antagonists
- Hydralazine and Nitrates
- Angiotensin II Receptor Blockers (ARBs) + Neprilysin Inhibitor

**Symptomatic benefit**
- Diuretics
- Digoxin


ENTRESTO™ (sacubitril/valsartan)

**Neprilysin Inhibitor (sacubitril)**

**Angiotensin Receptor Blocker (valsartan)**

**Indication:**
- reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction

Entresto™[prescribing information]. NJ. Novartis Pharmaceuticals; 8/2015.

How does Entresto™ work?

**Renin-Angiotensin-Aldosterone System**

- ANGIOTENSIN II
- ANGIOPOETIN
- VASODILATION

**Natriuretic Peptide System**

- NEPRILYSIN
- SACUBITRIL

Entresto™[prescribing information]. NJ. Novartis Pharmaceuticals; 8/2015.

ENTRESTO™ (sacubitril/valsartan) - Dosing


**Corlanor® (ivabradine)**

**Mechanism**
- Selective sinus-node inhibitor
- \( \downarrow \) spontaneous pacemaker activity at the sinus node by blocking hyperpolarization-activated cyclic nucleotide-gated (HCN) channel to selectively inhibit \( I_{\text{f}} \) current which \( \downarrow \) the heart rate
- Repolarization and contractility not affected

**Indication**
- To \( \downarrow \) the risk of hospitalization for worsening heart failure in patients with stable, symptomatic chronic heart failure with LVEF \( \leq 35\% \), who are in sinus rhythm with resting heart rate \( \geq 70 \) beats per minute and either are on maximally tolerated doses of beta-blockers or have a contraindication to beta-blocker use

**Corlanor® (ivabradine) - Dosing**

- 5 mg twice daily
- Can titrate in 2 weeks to maximum dose of 7.5 mg twice daily

<table>
<thead>
<tr>
<th>Heart Rate</th>
<th>Dose Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 60 bpm</td>
<td>Increase dose by 2.5 mg to max</td>
</tr>
<tr>
<td>50-60 bpm</td>
<td>Maintain dose</td>
</tr>
<tr>
<td>&lt; 50 bpm</td>
<td>Decrease dose by 2.5 mg, if currently on 2.5 mg discontinue therapy</td>
</tr>
</tbody>
</table>


Side Effects: Hypotension (18%), Hyperkalemia (12%), Dizziness (6%), Renal failure (5%), Angioedema (0.5%), Cough, *Itching

Corlanor® (ivabradine) [Prescribing Information]. Amgen; 2015.
Corlanor® (ivabradine) – Efficacy & Safety

<table>
<thead>
<tr>
<th>Effect</th>
<th>Corlanor® (n = 3,260) %</th>
<th>Placebo (n = 3,278) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradycardia</td>
<td>18% RRR</td>
<td>4.2% ARR</td>
</tr>
<tr>
<td>Hypertension, blood pressure increased</td>
<td>26% RRR</td>
<td>4.7% ARR</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>10</td>
<td>2.2</td>
</tr>
<tr>
<td>Phosphenes, visual brightness</td>
<td>8.3</td>
<td>6.6</td>
</tr>
<tr>
<td></td>
<td>2.8</td>
<td>0.5</td>
</tr>
</tbody>
</table>


In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.

ARNI should not be administered concomitantly with ACE inhibitors or within 36 hours of the last dose of an ACE inhibitor.

ARNI should not be administered to patients with a history of angioedema.

Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HFrEF (LVEF ≤35%) who are receiving GDEM, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest.


WHO Classifications of Pulmonary Hypertension (Etiology)

1. Pulmonary Arterial Hypertension
2. Left Heart Disease
3. Chronic Hypoxemia
4. Thromboembolic
5. Miscellaneous

Pulmonary Arterial Hypertension
**Pharmacologic - Classes**

**Prostacyclin pathway agonists**
- Epoprostenol
- Treprostinil
- Iloprost
- Selexipag

**Endothelin receptor antagonists (ERAs)**
- Ambrisentan
- Bosentan
- Macitentan
- Sildenafil
- Tadalafil
- Ritodrine

**PDE-5 inhibitors**
- Guanylate cyclase stimulant

**Nitric oxide-cyclic guanosine monophosphate enhancers**
- Iloprost
- Treprostinil IV
- Remodulin™ Tyvaso™ Orenitram®

**Oral Prostacyclin Therapy**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Treprostinil (Orenitram®)</th>
<th>Selexipag (Uptravi®)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosing</strong></td>
<td>0.125 mg Q 8 hours; may ↑ dose in increments of 0.25 mg or 0.5 mg Q 12 hours or 0.125 mg every 8 hours Q 3 to 4 days as tolerated to achieve optimal clinical response.</td>
<td></td>
</tr>
<tr>
<td><strong>Place in Therapy</strong></td>
<td>consider in patients with WHO functional class III symptoms</td>
<td></td>
</tr>
<tr>
<td><strong>Side effects</strong></td>
<td>headache, diarrhea, nausea, flushing, jaw pain, pain in extremity, hypokalemia, abdominal discomfort</td>
<td></td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td>wholesale acquisition cost for every 0.125mg is $4.88</td>
<td></td>
</tr>
</tbody>
</table>

**Administration**
- Continuous infusion (IV, SQ)
- Inhaled
- Oral

**Dose**
- 1.25 ng/kg/min
- 3 breaths (18 mcg per breath) four times daily during awake hours, titrate to max of 9 breaths
- 0.125 mg Q 8 hours; may increase dose in increments of 0.25 mg or 0.5 mg Q 12 hours or 0.125 mg every 8 hours Q 3 to 4 days as tolerated to achieve optimal clinical response

**Side effects**
- headache, diarrhea, nausea, flushing, jaw pain, pain in extremity, hypokalemia, abdominal discomfort
- headache, diarrhea, jaw pain, nausea, myalgia, vomiting, pain in extremity, flushing, arthralgia, anemia, decreased appetite, rash

**Cost**
- wholesale acquisition cost for each tablet is $130.68 to $290.40
- > $100,000 per year

**Adapted from Galie N, Corris PA, Frost et al. Updated treatment algorithm of pulmonary hypertension. In: UpToDate, Post (Ed), Waltham, MA. (Accessed on September, 2016.)**
Uptravi® (selexipag) - Mechanism

IP receptor: the only established relaxant prostanoid receptor in the human pulmonary artery

Established Prostanoid Receptors in the Human Pulmonary Artery

IP
EP_3
TP

Animal studies have shown...

The IP receptor promotes:
- Vasodilation
- Antiproliferation

EP, and TP receptors may cause:
- Vasoconstriction
- Cell proliferation

UPTRAVI® selectively targets the IP receptor

https://www.uptravi.com/hcp/uptravi/mechanism-of-action/

Uptravi® (selexipag) - Dosing

Other considerations:
- Take with food for tolerability
- Don't split, crush, chew
- Take missed dose immediately, unless next dose is within the next 6 hours
  If ≥ 3 days missed, restart at a lower dose and retitrate

Uptravi® (selexipag) - Efficacy

The Only Oral PAH Therapy Targeting the Prostacyclin Pathway Proven to Delay Disease Progression

<table>
<thead>
<tr>
<th>PATIENTS AT RISK</th>
<th>UPTAVI</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>574</td>
<td>852</td>
</tr>
<tr>
<td>1</td>
<td>455</td>
<td>433</td>
</tr>
<tr>
<td>2</td>
<td>381</td>
<td>347</td>
</tr>
<tr>
<td>3</td>
<td>246</td>
<td>220</td>
</tr>
<tr>
<td>4</td>
<td>171</td>
<td>149</td>
</tr>
<tr>
<td>5</td>
<td>101</td>
<td>86</td>
</tr>
<tr>
<td>6</td>
<td>40</td>
<td>28</td>
</tr>
</tbody>
</table>


COPD
What types of treatment/inhalers are there?

**Rescue Treatment**
- Short-acting COPD medicines that work quickly in case of sudden breathing problems
- Sometimes referred to as “quick relief” medications
- Relax airway muscles within minutes and are generally effective for about 4 to 6 hours
- SABA, SAMA

**Maintenance Treatment**
- Long-acting medicines taken daily to help prevent symptoms from occurring
- Treatments include 1 (monotherapy), 2 (dual therapy), or 3 (triple therapy) COPD medicines delivered in 1 or more inhalers
- LABA, LAMA, ICS

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How to Assess a Patient with COPD...

**Spirometrically Confirmed Diagnosis**
- Assessment of Airflow Limitation
  - FEV₁/FVC < 0.7

**Exacerbation History**
- ≥ 2 or ≥ 1 Leading to hospital admission
- 0 or 1 (NOT leading to hospital admission)

**Assessment of Symptoms / Risk of Exacerbations**
- mMRC 0-1 CAT < 10
- mMRC ≥ 2 CAT ≥ 10


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Manage Stable COPD: Pharmacologic Therapy

**RECOMMENDED FIRST CHOICE**

- ≥ 2 or ≥ 1 (leading to hospitalization)
- Not leading to hospitalization

**Mechanism of Action**
- Competitively and reversibly inhibits the action of acetylcholine at type 3 muscarinic (M₃) receptors in bronchial smooth muscle causing bronchodilation

**Dose**
- Oral nebulization inhalation solution: 175 mcg (1 unit-dose vial) once daily for maintenance COPD treatment

**Onset and Duration**
- Onset: within 45 minutes after single dose & peak FEV₁ effect is 2-3 hours following single dose
- Duration: up to 24 hours


**Yupelri (revefenacin)**
- FDA Approval Date November 09, 2018
- the first and only once-daily, nebulized bronchodilator approved for COPD in the US

**Mechanism of Action**
- Oral nebulization inhalation solution: 175 mcg (1 unit-dose vial) once daily for maintenance COPD treatment

**Onset and Duration**
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- Duration: up to 24 hours

**FDA Approval Date November 09, 2018**
- the first and only once-daily, nebulized bronchodilator approved for COPD in the US"
Yupelri (revefenacin)

Adverse Effects Special Considerations

Hypertension
• Does not require dilution prior to administration - Do not mix with other medications in nebulizer
• If paradoxical bronchospasm occurs, manage with a SABD, discontinue revefenacin, and institute alternative therapy
• Use with caution in patients with narrow-angle glaucoma; may ↑ intraocular pressure.
• Use with caution in patients with prostatic hyperplasia or bladder neck obstruction; may cause and/or worsen urinary retention.
• Cost (30 ds): $320 - $400

Headache

Dizziness

Back pain

Nasopharyngitis

URI

Oropharyngeal pain

Paradoxical bronchospasm

Follow-Up Recommendations

1. If response to initial treatment is appropriate, maintain initial treatment.
2. If Not:
   • Consider the predominant treatable trait to target (Dyspnea vs Exacerbations)
   • Use exacerbation pathway if both exacerbations and dyspnea need to be targeted
   • Place patient in box corresponding to current treatment & follow indications
   • Assess, Adjust, and Review response
   These recommendations do not depend on the ABCD assessment at diagnosis

Managing COPD with 3 Medicines in 1

Reduce Inflammation
ICS (anti-inflammatory)
↓ inflammation & swelling in lungs

Open Airways
LABA (bronchodilator) opens airways by relaxing muscles around the airways in lungs

Keep Airways Open
LAMA (bronchodilator) blocks tightening of smooth muscle around airways

Inhaled Corticosteroids

<table>
<thead>
<tr>
<th>Agent</th>
<th>Combo product</th>
<th>Dose (mcg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Budesonide</td>
<td>+ formoterol (MDI, Symbicort)</td>
<td>160/4.5 mcg/inhalation - 2 inhalations BID</td>
</tr>
<tr>
<td></td>
<td>+ salmeterol (DPI Advair)</td>
<td>250/50 mcg/inhalation - 1 inhalation BID</td>
</tr>
<tr>
<td>Fluticasone</td>
<td>+ vilanterol (DPI, Breo Ellipta)</td>
<td>100/25 mcg/inhalation - 1 inhalation daily</td>
</tr>
<tr>
<td></td>
<td>+ vilanterol + umeclidinium (Trelegy Ellipta)</td>
<td>1 oral inhalation of fluticasone furoate 100 mcg/umeclidinium 62.5 mcg/vilanterol 25 mcg once daily</td>
</tr>
</tbody>
</table>

No clinical benefit of one over another
• Linked to increase risk of pneumonia in COPD
Trelegy Efficacy

![Comparison of Trelegy vs FF/VI and UMEC/VI](https://gsksource.com/pharma/content/gsk/source/us/en/brands/trelegy/pi/efficacy.html)

**Systemic/Oral Corticosteroids**
- Hyperglycemia
- HPA axis suppression
- Osteoporosis

**Inhaled Corticosteroids**
- Oral candidiasis (dose dependent)
- Dysphonia (steroid induced myopathy of vocal cords), hoarse voice, skin bruising, PNA

**Systemic side effects (dose dependent):**
- Pneumonia
- Hoarseness
- Sore throat
- Skin bruising
- HPA axis suppression
- Osteoporosis
- Cataract formation
- Growth suppression (can occur at ↓ doses)

**Minimize systemic exposure**
- Use spacers with MDI ➔ Additionally will reduce oral side effects
- Rinse mouth with water and spit after use to reduce risk of oral candidiasis

---

Patient Case – back to CD

CD is a 65 year old female presenting to clinic today for a hospital follow-up. She ended up in the hospital for what was termed a COPD exacerbation and a newly diagnosed HF hospitalization. She sometimes has worsening shortness of breath which she notices mostly at work (chef x 30 years). She says she used to be able to carry heavy loads with no problem, however she has trouble breathing and this makes her job more difficult. She reports that she used to smoke, but has actually quit smoking cold turkey since being out of the hospital. She endorses a nagging cough for the past several years that she always attributed to smoking. Her echocardiogram revealed an LVEF 30%. She states that her breathing has not gotten any better since being out of the hospital and they did not change anything about her COPD regimen. She has been in the hospital x 1 this year for COPD and the heart failure is new to her. Remember, she was previously diagnosed with Atrial Fibrillation. She prefers you not to add another inhaler or another medication, but knows something needs to be done in regard to her COPD, possibly her HF. Some labwork and spirometry are obtained at this visit as well.

**Current Medication List:**
- Albuterol (SABA) 1 puff every 4-6 hours PRN
- Aspirin 81 mg daily
- Atorvastatin 40 mg each evening
- Carvedilol 12.5 mg BID
- Eliquis 5 mg BID
- Furosemide 20 mg daily
- Lisinopril 5 mg daily
- Stiolto Respimat (Tiotropium + Olodaterol) (LAMA + LABA) 2 inhalations once daily

**PMH:**
- Atrial Fibrillation
- COPD
- Dyslipidemia
- Heart Failure with reduced EF (30% EF)
- History of MI
- Hypertension

**Vitals from today:**
- Height: 65 inches
- Weight: 120 lbs
- Blood Pressure: 135/90
- Heart Rate: 70 bpm
- O2 Saturation: 97%
Patient Case – back to CD

### Spirometry

<table>
<thead>
<tr>
<th></th>
<th>Pre-bronchodilator</th>
<th></th>
<th>Post-bronchodilator</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Actual</td>
<td>%</td>
<td>Predicted</td>
<td>%</td>
</tr>
<tr>
<td>FEV₁</td>
<td>3.1 L</td>
<td>80%</td>
<td>3.15 L</td>
<td>83%</td>
</tr>
<tr>
<td>FEV₁/FVC (%)</td>
<td>68%</td>
<td></td>
<td>60%</td>
<td></td>
</tr>
</tbody>
</table>

### COPD Assessment Test (CAT)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shortness of breath after minimal activity</td>
<td>3</td>
</tr>
<tr>
<td>Frequent wheezing</td>
<td>2</td>
</tr>
<tr>
<td>CO₂ retention</td>
<td>1</td>
</tr>
<tr>
<td>Dyspnea during daily activities</td>
<td>0</td>
</tr>
<tr>
<td>Dry cough</td>
<td>0</td>
</tr>
<tr>
<td>Nocturnal symptoms</td>
<td>0</td>
</tr>
</tbody>
</table>

Labwork from today:

- WBC: 11.0 x 10⁹/L
- Eosinophils: 220 cells/µL
- BUN: 20 mg/dL
- SCR: 1.0 mg/dL
- K⁺: 4.0 mEq/L
- Glucose: 99 mg/dL
- Cholesterol, Total: 125 mg/dL
- Triglycerides: 140 mg/dL
- HDL: 45 mg/dL
- VLDL: 28 mg/dL
- LDL: 52 mg/dL

What would you do for CD regarding her Heart Failure?

A. Add Corlanor 5 mg twice daily.
B. Increase Lisinopril from 5 mg to 10 mg daily.
C. Discontinue Furosemide 20 mg daily.
D. Discontinue Lisinopril. Initiate Entresto 36 hours later.

What would you do for CD regarding her COPD?

A. Continue Stiolto Respimat, but increase the dose to 2 inhalations twice daily.
B. Add Prednisone x 1 week.
C. Discontinue Stiolto Respimat. Initiate Trelegy Ellipta, one inhalation once daily.
D. Increase Albuterol usage to every 2 hours.

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