

New and Novel Medications for Respiratory Care

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Objectives

- ▶ Quick overview of the newest FDA-approved respiratory-related medications
 - ▶ Inhalers
 - ▶ Injectables
 - ▶ Oral medications

Conflicts of Interest

- ▶ I have no conflicts of interest to disclose

List of medications to be discussed

- ▶ Bevespi Aerosphere
- ▶ Utibron Neohaler
- ▶ Stiolto/Striverdi Respimat
- ▶ Arnuity Ellipta
- ▶ Incruse Ellipta
- ▶ Anoro Ellipta
- ▶ Breo Ellipta
- ▶ Trelegy Ellipta
- ▶ Symdeko (tezacaftor/ivacaftor)
- ▶ Cinqair (reslizumab)
- ▶ Nucala (mepolizumab)
- ▶ Orkambi (lumacaftor/ivacaftor)
- ▶ Esbriet (pirfenidone)
- ▶ Ofev (nintendanib)
- ▶ Adempas (riociguat)
- ▶ Opsumit (macintentan)

Bevespi Aerosphere

- ▶ Combination of glycopyrrolate and formoterol fumarate
 - ▶ Formoterol: LABA mainly used in combination inhalers
 - ▶ Remember Foradil? No longer available in US
 - ▶ Glycopyrrolate: Muscarinic anticholinergic with new formulation as an inhaled medication
- ▶ Approved 2016 for Chronic Obstructive Pulmonary Disease
 - ▶ Black box warning: not for asthma treatment

Bevespi Aerosphere

- ▶ Delivery device: pressurized MDI
- ▶ Dose: Two inhalations twice a day
- ▶ Phospholipid-based CO-SUSPENSION delivery technology
 - ▶ Drug is adhered to miniature "cells"
 - ▶ 9 mcg glycopyrrolate + 4.8 mcg formoterol fumarate

Bevespi Aerosphere

- ▶ Drug Trials (Phase IIIb)
 - ▶ Improves peak FEV₁
 - ▶ Increases predose FEV₁ by 150mL at 24 weeks
 - ▶ Inspiratory capacity increased by 381mL
 - ▶ *All vs placebo

<https://www.bevespi-aerosphere.com/ama-labo-dual-bronchodilation.html>

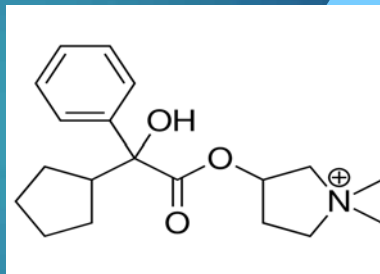
Glycopyrrolate

First indicated for preop use to reduce salivary, tracheobronchial, and pharyngeal secretions

Does not cross blood-brain barrier so no hallucinations/sedation

Inhaled/aerosolized glycopyrrolate study dates back to 1990

M3 receptors in proximal airways



<https://upload.wikimedia.org/Glycopyrrolate>

Gilman MJ, Meyer L, Carter J, Slovis C (November 1990). "Comparison of aerosolized glycopyrrolate and metaproterenol in acute asthma". *Chest*. 98 (5): 1095–8

Long Acting Muscarinic Antagonists

- ▶ Pharmacokinetics
 - ▶ Onset of action: rapid
 - ▶ Peak effect: 5-15 minutes
 - ▶ Duration: 33-53 hours (glycopyrrolate)
- ▶ Indicated for solely for COPD

[commons.wikimedia.org/Umeclidinium.svg](https://commons.wikimedia.org/wiki/File:Umeclidinium.svg)

Utibron Neohaler

- ▶ Combination of indacaterol and glycopyrrolate
 - ▶ Indacaterol brand name Arcapta
- ▶ Dose: one inhalation twice a day
- ▶ Indacaterol classified as an *ultra*-LABA
- ▶ Approved October 2015



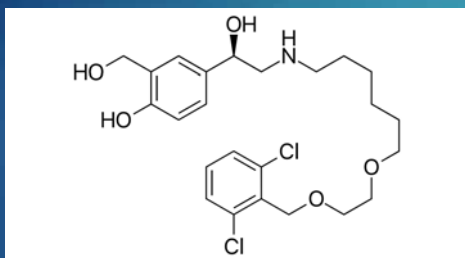
www.utibron.com

Ultra-LABA

- ▶ Pharmacokinetics:
 - ▶ Onset of action: 5 minutes
 - ▶ Peak effect: 1-4 hrs
 - ▶ Duration of action: 24 hours
- ▶ Pharmacology:
 - ▶ Gets onto receptor, large molecular size keeps it there

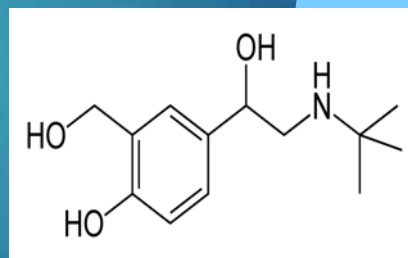
Ultra-LABA vs Albuterol

Vilanterol



[wikimedia.org/commons/Vilanterol.svg](https://commons.wikimedia.org/wiki/File:Vilanterol.svg)

Albuterol



[wikimedia.org/commons/albuterol.svg](https://commons.wikimedia.org/wiki/File:Albuterol.svg)

Neohaler delivery device

- ▶ The 3 I's
 - ▶ Insert
 - ▶ Inhale
 - ▶ Inspect



<http://www.uilbron.com/how-to-use-uilbron.html>

Stiolto/Striverdi Respimat

- ▶ Stiolto is a combination of tiotropium bromide and olodaterol
 - ▶ Approved May 2015
- ▶ Olodaterol: *ultra*-LABA approved in 2013 as Striverdi
- ▶ Approved May 2015 for maintenance of COPD

Olodaterol

- ▶ Pharmacokinetics
 - ▶ Onset: 5 minutes
 - ▶ Peak effect: 10-20 minutes
 - ▶ Duration of action: 24 hours

Respimat Delivery Device

- ▶ Soft mist inhaler developed by Boehringer Ingelheim
 - ▶ Also available with Spiriva and Combivent in the US
- ▶ Delivers more drug into lungs vs MDI
 - ▶ 53% vs 21% per mfgr study



<http://www.boehringer-ingelheim.com/respimat.png>

The Elliptas

- ▶ Arnuity (Fluticasone) Ellipta
- ▶ Incruse (Umeclidinium) Ellipta
- ▶ Anoro (Umeclidinium and vilanterol) Ellipta
- ▶ Breo (Fluticasone and vilanterol) Ellipta
- ▶ Trelegy (fluticasone, umeclidinium, vilanterol) Ellipta

Ellipta Delivery Device

- ▶ Developed by GlaxoSmithKline
- ▶ Very similar to Diskus (same engineer developed both)
- ▶ Has two strips that activate once the device is used



<https://www.gsk.com/en-GB/behind-the-science/our-people/making-the-ellipta-inhaler-a-reality/>

Ellipta Delivery Device

- ▶ Using the device: open cover until it clicks, then inhale dose
- ▶ Closing the cover 'resets' the device and prepares another dose
- ▶ Dual strip med packets allow smaller inhaler size



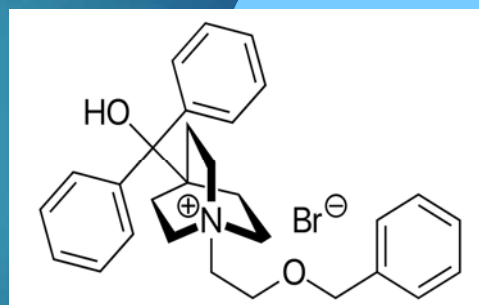
reddituploads.com

Arnuity (Fluticasone furoate)

- ▶ Indicated for asthma
 - ▶ Available as 100mcg or 200mcg doses
 - ▶ Steroid – must rinse mouth after use
- ▶ Approved August 2014

Incruse Ellipta (Umeclidinium)

- ▶ Long-acting muscarinic antagonist (LAMA)
- ▶ Indicated for COPD
- ▶ Dose: one inhalation of 62.5mcg daily
- ▶ Approved May 2014



[commons.wikimedia.org/umeclidinium.svg](https://commons.wikimedia.org/wiki/File:Umeclidinium.svg)

Anoro (umeclidinium and vilanterol)

- ▶ Added vilanterol to Incruse
 - ▶ *Ultra*-LABA
 - ▶ Indicated for COPD
- ▶ Dose: one inhalation of umeclidinium 62.5 mcg/vilanterol 25mcg once daily
- ▶ Approved December 2013

Breo (fluticasone and vilanterol)

- ▶ Combined Arnuity with vilanterol
 - ▶ *Ultra-LABA* plus steroid
 - ▶ Indicated for both asthma and COPD
- ▶ Dose: one inhalation of fluticasone 100 or 200mcg/vilanterol 25mcg once daily
- ▶ Approved May 2013

Trelegy (umeclidinium, fluticasone, and vilanterol)

- ▶ Combined Arnuity with Anoro (THEY DID IT)
 - ▶ *Ultra-LAMA* plus *Ultra-LABA* plus steroid
 - ▶ Indicated for COPD
- ▶ Dose: one inhalation of fluticasone 100mcg/vilanterol 25mcg/umeclidinium 62.5mcg once daily
- ▶ Approved September 2017

Non-Inhaled Medications

Symdeko (tezacaftor/ivacaftor)

- ▶ Available as an oral tablet
- ▶ Indicated for Cystic Fibrosis (specific CFTR mutations) for patients >12 years of age
- ▶ Pharmacologic class: CF transmembrane conductance regulator corrector/potentiator
- ▶ Dose: tezacaftor 100mg/ivacaftor 150mg in AM, ivacaftor 150mg in evening

Symdeko (tezacaftor/ivacaftor)

- ▶ Mechanism of actions
 - ▶ Tezacaftor: Improves conformational stability resulting in increased trafficking and processing of mature protein to cell surface
 - ▶ Ivacaftor: increased chloride transport by potentiating the channel-open probability

Symdeko (tezacaftor/ivacaftor)

- ▶ Adverse reactions:
 - ▶ elevated liver enzymes
 - ▶ distal intestinal obstruction syndrome
- ▶ Cost: \$26,880 for 30 days
- ▶ What you should look for: patients complaining of dizziness or severe abdominal pain

Orkambi (lumacaftor/ivacaftor)

- ▶ Also available in an oral formulation
- ▶ Dose: lumacaftor 400mg/ivacaftor 250mg twice a day
- ▶ Pharmacologic class: same as Symdeko
- ▶ Approved July 2015

Orkambi (lumacaftor/ivacaftor)

- ▶ Adverse reactions:
 - ▶ Chest discomfort (22% in postmarketing case reports)
 - ▶ Elevated liver enzymes
- ▶ Cost: \$6,275 for 30 days
- ▶ What you should look for: pharyngitis

Cinqair (reslizumab)

- ▶ Available as an intravenous injection
- ▶ Indicated for Asthma
- ▶ Approved March 2016
- ▶ Pharmacologic class: IL-5 receptor antagonist
 - ▶ Responsible for growth, recruitment, activation of eosinophils
- ▶ Dose 3mg/kg once every 4 weeks

Cinqair (reslizumab)

- ▶ Add-on maintenance treatment for adults with an eosinophilic phenotype
- ▶ IV infusion over 20-50 minutes
- ▶ Asses improvement with peak flow tests
- ▶ Cost: \$2,700 per month
- ▶ What you should look for: patients may experience throat pain

Nucala (mepolizumab)

- ▶ Available as a subcutaneous injection
- ▶ Indicated for Asthma
 - ▶ Also for eosinophilic granulomatosis with polyangiitis
- ▶ Approved November 2015
- ▶ Pharmacologic class: IL-5 receptor antagonist
- ▶ Dose 100mg once every 4 weeks

Nucala (mepolizumab)

- ▶ Assess improvement with PFTs, peak flow, FEV₁
- ▶ Cost: one month \$3400
- ▶ What you should look for: patient using rescue inhalers more often – may be indicative of worsening asthma

Esbriet (pirfenidone)

- ▶ Available in an oral formulation
- ▶ Indicated for treatment of Idiopathic Pulmonary Fibrosis
- ▶ Approved October 2014
- ▶ Pharmacologic class: anti-inflammatory, antifibrotic
 - ▶ MOA unknown; may decrease fibroblast proliferation and fibrosis-associated proteins and cytokines

Esbriet (pirfenidone)

- ▶ Dose: Induction schedule
 - ▶ Day 1-7: 267mg three times a day
 - ▶ Day 8-14: 534mg TID
 - ▶ Day 15 and on: 801mg TID

Esbriet (pirfenidone)

- ▶ Adverse reactions: fatigue and headache
- ▶ Cost: \$10,221/month
- ▶ What you should look for: may cause upper resp tract infections, dyspnea, cough, and throat irritation.

Ofev (nintendanib)

- ▶ Available as an oral tablet
- ▶ Indicated for treatment of Idiopathic Pulmonary Fibrosis
- ▶ Approved October 2014
- ▶ Pharmacologic class: Tyrosine Kinase Inhibitor

Ofev (nintedanib)

- ▶ Adverse reactions: dose may need to be reduced if patient has bad GI toxicity
- ▶ Cost: \$10,990/month
- ▶ What you should look for: patients may get bronchitis (<1% in postmarketing studies), main issue is with severe gastrointestinal distress causing patients to stop taking med until it resolves

Adempas (riociguat)

- ▶ Available in oral formulation
- ▶ Indicated for both chronic thromboembolic pulmonary hypertension and pulmonary arterial hypertension
- ▶ Approved October 2013
- ▶ Pharmacologic class: soluble guanylate cyclase stimulator

Adempas (riociguat)

- ▶ Adverse effects: Hypotension in 3-10%
- ▶ Cost: \$5,461
- ▶ What you should look for: hemoptysis can occur

Opsumit (macitentan)

- ▶ Available as a 10mg oral tablet
- ▶ Indicated for pulmonary arterial hypertension
- ▶ Approved October 2013
- ▶ Pharmacologic class: Endothelin Receptor Antagonist, vasodilator

Opsumit (macitentan)

- ▶ Adverse effects: Hypotension in 3-10%
- ▶ Cost: \$5,418
- ▶ What you should look for: hemoptysis can occur

Questions?

