

A Breath of Fresh Air: Updates in COPD Management

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The speaker has nothing to disclose

Abbreviations

- COPD: Chronic obstructive pulmonary disease
- GOLD: Global initiative for chronic Obstructive Lung Disease
- FEV1: Forced expiratory volume in 1 second
- FVC: Forced vital capacity
- ICS: Inhaled corticosteroid
- LABA: Long-acting β_2 -agonist
- LAMA: Long-acting muscarinic antagonist
- TDI: Transition dyspnoea index
- mMRC: Modified British Medical Research Council (mMRC) Questionnaire
- CAT: COPD Assessment Test
- SGRQ: St. George's Respiratory Questionnaire

Abbreviations for Inhaler Components

- ACL: acclidinium
- FP: fluticasone propionate
- GLY: glycopyrrolate/glycopyrronium
- OLO: olodaterol
- SAL: salmeterol
- TIO: tiotropium
- UMEC: umeclidinium
- VI: vilanterol

Test Your Inhaler Knowledge

What is the brand name for umeclidinium?

- A. Symbicort®
- B. Incruse®
- C. Tudorza™
- D. Stiolto™

What type of device is Aracapta™
(indacaterol)?

- A. Diskus®
- B. Respimat®
- C. Neohaler™
- D. Ellipta®

What class(es) of medication(s) are found in Stiolto™?

- A. LAMA/LABA
- B. ICS/LABA
- C. LAMA only
- D. LABA only

What is the brand name for fluticasone propionate/salmeterol?

- A. Dulera®
- B. Utibron™
- C. Flovent®
- D. Advair®

What type of device is Breo® (fluticasone furoate/vilanterol)?

- A. Diskus®
- B. Respimat®
- C. MDI
- D. Ellipta®

What class of medications is in Spiriva®?

- A. LAMA/LABA
- B. ICS/LABA
- C. LAMA only
- D. LABA only

Objectives

Pharmacists:

- List recent changes to the GOLD guidelines
- Recall efficacy and safety of long-acting muscarinic antagonist (LAMA)/long-acting beta-agonist (LABA) combination therapy
- Recognize new inhaler devices and products for COPD

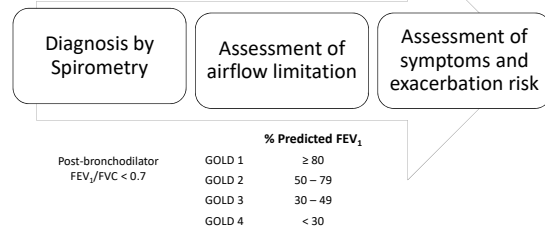
Technicians:

- List recent changes to the GOLD guidelines
- Recall new devices and products for COPD
- Classify new medications according to drug classes

What is Chronic Obstructive Pulmonary Disease (COPD)?

- Chronic airflow limitation
- Caused by cumulative environmental exposures and host factors
 - Smoking
 - Genetics
 - Airway hyper-responsiveness
 - Poor lung growth during childhood
- 4th leading cause of death in the world

Diagnosis of COPD



GOLD Guidelines 2018 Update

Modified British Medical Research Council (mMRC) Questionnaire

mMRC Grade 0	I only get breathless with strenuous exercise
mMRC Grade 1	I get short of breath when hurrying on the level or walking up a slight hill
mMRC Grade 2	I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level
mMRC Grade 3	I stop for breath after walking about 100 meters or after a few minutes on the level
mMRC Grade 4	I am too breathless to leave the house or I am breathless when dressing or undressing

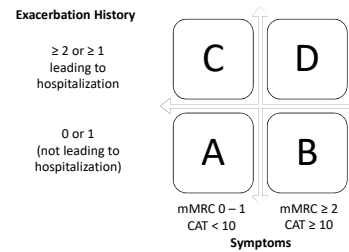
GOLD Guidelines 2018 Update

COPD Assessment Test (CAT™)

I never cough	0 1 2 3 4 5	I cough all the time
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up on a hill or one flight of stairs I am very breathless
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition
I have lots of energy	0 1 2 3 4 5	I have no energy at all

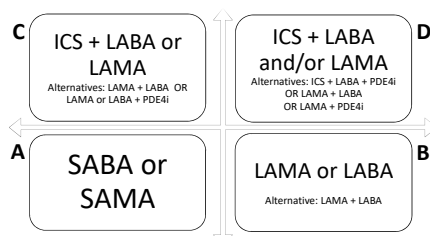
GOLD Guidelines 2018 Update

Assessment of Symptoms and Exacerbation Risk



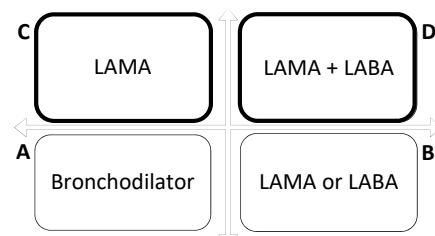
GOLD Guidelines 2018 Update

Pharmacologic Treatment for Stable COPD



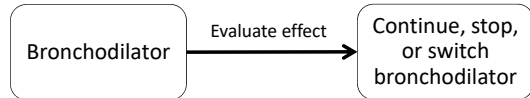
GOLD Guidelines 2016 Update

Updated Preferred Pharmacologic Treatment for Stable COPD



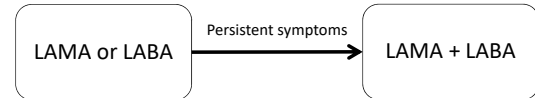
GOLD Guidelines 2018 Update

Group A



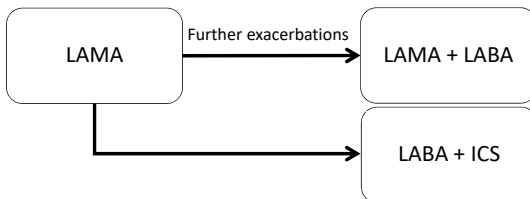
GOLD Guidelines 2018 Update

Group B



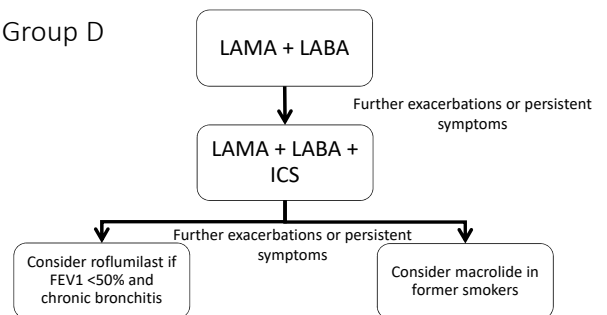
GOLD Guidelines 2018 Update

Group C



GOLD Guidelines 2018 Update

Group D



GOLD Guidelines 2018 Update

What happened to inhaled corticosteroids?

LAMA/LABA vs LABA/ICS:
Airway Markers

BMC Pulm Med 2015;15:91.
Respir Med 2015;109:870-881.
Eur Respir J 2016;48:1030-1039.

Lancet Respir Med 2013;1:51-60.
Int J Chron Obstruct Pulmon Dis 2015;10:1015-1026.
N Engl J Med 2016;374:2222-2234.

Study	Treatment Arms (n)	Population	Study Outcomes	P-value
Singh et al, 2015	UMEC/VI 62.5/25mcg daily (334) SAL /FP 50/500mcg BID (340)	FEV ₁ 30-70% mMRC ≥ 2 ≤ 1 exacerbation in previous year	• Change in FEV ₁ : 0.166L v 0.87L • Trough FEV ₁ : 1.6L v 1.511L • Increased patients with trough FEV ₁ ≥100mL	<0.001 <0.001 <0.001
Donohoe et al, 2015	UMEC/VI 62.5/25mcg daily (353) SAL/FP 50/250mcg BID (353)	FEV ₁ 30-70% mMRC ≥ 2 No exacerbation in previous year	• FEV ₁ : 40.074L • Trough FEV ₁ : 1.488L v 1.406L • Patients improving ≥100mL: 59% v 42%	<0.001 <0.001 <0.001
Donohoe et al, 2015	UMEC/VI 62.5/25mcg daily (349) SAL/FP 50/250mcg BID (348)	FEV ₁ 30-70% mMRC ≥ 2 No exacerbation in previous year	• FEV ₁ : 40.101L • Trough FEV ₁ : 1.499L v 1.401L • Patients improving ≥100mL: 64% v 45%	<0.001 <0.001 <0.001
Vogelmeier et al, 2016	ACL/FOR 400/12mcg BID (468) SAL/FP 50/500mcg BID (463)	FEV ₁ < 80% CAT score ≥ 10 Exacerbation in previous 6 months	• Peak FEV ₁ : 493mL • Trough FEV ₁ : 1.405L v 1.419L	<0.001 0.36
Vogelmeier et al, 2013	IND/GLY 110/50mcg daily (258) SAL/FP 50/500mcg BID (264)	GOLD II & III FEV ₁ 40-80% No exacerbations in previous year	• FEV ₁ AUC _{0-12h} : 1.695L v 1.557L • Trough FEV ₁ : 1.601L v 1.498L	0.026 0.025
Zhong et al, 2015	IND/GLY 110/50mcg daily (343) SAL/FP 50/500mcg BID (333)	GOLD II & III mMRC ≥ 2 ≤ 1 exacerbation in previous year	• Trough FEV ₁ : 475mL • Patients improving ≥100mL: 61% v 44%	<0.001 --
Wedzicha et al, 2016	IND/GLY 110/50mcg daily (1680) SAL/FP 50/500mcg BID (1682)	mMRC ≥ 2 FEV ₁ 25-60% ≥1 exacerbation in previous year	• Trough FEV ₁ : 462mL • FEV ₁ AUC _{0-12h} : 1.110mL	0.003 <0.001

LAMA/LABA vs LABA/ICS: Symptom Control

BMC Pulm Med 2015;15:91.
Respir Med 2015;109:870-881.
Eur Respir J 2016;48:1030-1039.

Lancet Respir Med 2013;1:51-60.
Int J Chron Obstruct Pulmon Dis 2015;10:1015-1026.
N Engl J Med 2016;374:2222-2234.

Study	Treatment Arms (n)	Study Outcomes	P-value
Singh et al, 2015	UMEC/VI 62.5/25mcg daily (334) SAL /FP 50/500mcg BID (340)	• Change in SGRQ score: -5.10 v -5.64 • Change in CAT score: -2.21 v -2.35 • Rescue medication use/day: 2.0 v 1.7	0.545 -- 0.078
Donohoe et al, 2015	UMEC/VI 62.5/25mcg daily (353) SAL/FP 50/250mcg BID (353)	• Similar clinical reductions in TDI & SGRQ scores • Similar reductions in puffs of rescue medication/day	-- --
Donohoe et al, 2015	UMEC/VI 62.5/25mcg daily (349) SAL/FP 50/250mcg BID (348)	• Similar clinical reductions in TDI & SGRQ scores • Reduction in puffs of rescue medication/day	-- <0.05
Vogelmeier et al, 2016	ACL/FOR 400/12mcg BID (468) SAL/FP 50/500mcg BID (463)	• AECOPD: 15.8% v 16.6% • Change in SGRQ score: -4.7 v -5.7	0.98 0.27
Vogelmeier et al, 2013	IND/GLY 110/50mcg daily (258) SAL/FP 50/500mcg BID (264)	• TDI increase ≥1: 67.5% v 56.8% • Increased % days with no daytime symptoms • Reduced rescue medication use	0.003 0.049 0.019
Zhong et al, 2015	IND/GLY 110/50mcg daily (343) SAL/FP 50/500mcg BID (333)	• Annualized COPD exacerbation rate: RR 0.69 • Annualized COPD exacerbation rate in patients with history of exacerbation: RR 0.60 • Prolonged time to first exacerbation	<0.05 0.028 --
Wedzicha et al, 2016	IND/GLY 110/50mcg daily (1680) SAL/FP 50/500mcg BID (1682)	• AECOPD rate: 3.59 v 4.03 • Time to first exacerbation: 71d v 51d • Rate of moderate to severe exacerbation: 0.98 v 1.19 • Patients with significant decrease in SGRQ: 49% v 44%	0.003 <0.001 <0.001 <0.001

LAMA/LABA vs LABA/ICS: Adverse Events

BMC Pulm Med 2015;15:91.
Respir Med 2015;109:870-881.
Eur Respir J 2016;48:1030-1039.

Lancet Respir Med 2013;1:51-60.
Int J Chron Obstruct Pulmon Dis 2015;10:1015-1026.
N Engl J Med 2016;374:2222-2234.

Study	Treatment Arms (n)	Study Outcomes
Singh et al, 2015	UMEC/VI 62.5/25mcg daily (334) SAL /FP 50/500mcg BID (340)	• Treatment-related AEs: 2% v 4% • Serious AEs: 2% v <1% • Pneumonia: 0 v < 1%
Donohoe et al, 2015	UMEC/VI 62.5/25mcg daily (353) SAL/FP 50/250mcg BID (353)	• Drug-related AEs: 2% v 2% • AEs leading to discontinuation: 2% v 3%
Donohoe et al, 2015	UMEC/VI 62.5/25mcg daily (349) SAL/FP 50/250mcg BID (348)	• Drug-related AEs: 2% v 2% • AEs leading to discontinuation: 2% v 3%
Vogelmeier et al, 2016	ACL/FOR 400/12mcg BID (468) SAL/FP 50/500mcg BID (463)	• AE leading to discontinuation: 5.6% v 7.3% • Pneumonia: 0.6% v 1.9% • Serious cardiac events: 0.9% v 0.4%
Vogelmeier et al, 2013	IND/GLY 110/50mcg daily (258) SAL/FP 50/500mcg BID (264)	• Worsening COPD: 17.1% v 23.5% • Pneumonia: 0% v 1.5% • Upper respiratory infections: 2.7% v 0.8% • AEs leading to discontinuation: 8.5% v 10.2%
Zhong et al, 2015	IND/GLY 110/50mcg daily (343) SAL/FP 50/500mcg BID (333)	• COPD-related AE: 20.2% v 26.3% • Pneumonia: 0.8% v 2.7% • Upper respiratory infections: 3.5% v 7.0% • AEs leading to hospitalizations: 4.3% v 8.4%
Wedzicha et al, 2016	IND/GLY 110/50mcg daily (1680) SAL/FP 50/500mcg BID (1682)	• Worsening COPD: 77.4% v 81.1% • Pneumonia: 3.2% v 4.8% (p 0.02) • AE leading to discontinuation: 7.5% v 8.5%

Cardiovascular Concerns



COPD patients beginning inhaler therapy at greater short-term risk ...
Cardiovascular Business - Jan 3, 2018
People with **chronic obstructive pulmonary disease (COPD)** who used long-acting inhaled bronchodilators for the first time demonstrated a 50 percent heightened risk of **cardiovascular disease (CVD)** in the first 30 days after taking the medicine, according to a study published in JAMA Internal Medicine.



GSK Submits Landmark IMPACT Data to European Medicines ...
Business Wire (press release) - Feb 14, 2018
IMPACT is the first study to directly compare three commonly used COPD combination treatment classes delivered using the same dose and inhaler. ... Beta2-adrenergic agonists may produce significant hypokalaemia in some patients, which has the potential to produce adverse cardiovascular effects.

Starting new **COPD inhaler** tied to **heart attack risk**
Reuters - Jan 2, 2018
(Reuters Health) - People with **chronic obstructive pulmonary disease (COPD)** who use long-acting inhaled bronchodilators may have an increased risk of **heart attacks** and **strokes** right after they start taking these medicines, a Taiwanese study suggests. **COPD** is usually caused by smoking, and symptoms ...

JAMA Intern Med 2018; 178(2):229-238

Reframing Cardiovascular Controversies

- Are we unmasking undiagnosed cardiovascular problems?
- What about the conflicting evidence?
 - Improvements in left ventricular end diastolic volume with LAMA/LABA use
 - Excellent cardiovascular profile in clinical trials of LAMA/LABA
 - Lower cardiovascular risk compared to LABA/ICS

Lancet Respir Med 2018; e-pub ahead of print
Int J Chron Obstruct Pulmon Dis 2017; 12:3409-3485
Ann Pharmacother 2017; 51(11):985-993

Critique

- Clinical significance of selected endpoints
- Doses of LAMA/LABA studied & approved
- Use of old GOLD classifications
- Limited population with significant history of moderate to severe exacerbations

Summary of Data

- LAMA/LABA offers significant improvements in FEV₁ over LABA/ICS
- Decreases in acute exacerbations of COPD
- Increased time to first exacerbation
- Similar to improved reported symptom control and rescue inhaler use
- Similar adverse events with one report of significantly less pneumonia with LAMA/LABA

What inhalers are available?

Available Devices

- | | |
|--------------------------------|-------------------------|
| • Metered dose inhalers (MDIs) | • Respimat [®] |
| • Diskus [®] | • Ellipta [®] |
| • Flexhaler [®] | • Neohaler [®] |
| • Twisthaler [®] | • Pressair |
| • HandiHaler [®] | |

Respimat[®] Inhalation Use

1. Hold device upright.
2. Turns clear base in direction of arrows until it clicks (half turn)
3. Flip cap open until it snaps
4. Breathes out fully
5. Breathes out away from device
6. Puts device into mouth
7. Keep device horizontal
8. Tightly seals lips around mouthpiece opening
9. Do not cover air vents
10. Presses the dose release button (while taking in slow deep breath)
11. Continues to breathe in slowly for as long as possible
12. Holds breath for at least 5 seconds
13. Removes device from mouth
14. Breath normally
15. Closes the device cap

Adapted from University of Chicago's COPD Training Documents

Ellipta® Inhalation Technique

1. Opens the device until the mouthpiece appears
2. Breathes out fully
3. Breathes out away from device
4. Tightly seals lips around mouthpiece opening
5. Does not cover air vent
6. Takes a deep breath to take in medicine
7. Holds breath for at least 5 seconds
8. Removes device from mouth
9. Breathes normally
10. Closes device

Adapted from University of Chicago's COPD Training Documents

Neohaler® Inhalation Use

1. Pull off cap
2. Open inhaler by tilting the mouthpiece
3. Remove capsule from foil package
4. Insert capsule into chamber
5. Close the inhaler until it clicks
6. Pierce capsule ONCE and release
7. Breathe out fully
8. Breathe out away from device
9. Tightly seal lips around the mouthpiece
10. Inhale quickly and deeply
11. Hold breath for at least 5 seconds
12. Repeat steps 7-11 to ensure full dose is received
13. Remove capsule and discard
14. Close device

Adapted from University of Chicago's COPD Training Documents

Pressair® Inhalation Technique

1. Removes cap
2. Presses and releases green button (colored control window is now green)
3. Breathes out fully
4. Breathes out away from device
5. Keeps device horizontal throughout inhalation
6. Tightly seals lips around mouthpiece opening
7. Inhales quickly and deeply creating click sound
8. Holds breath for at least 5 seconds
9. Removes device from mouth
10. Breathes normally
11. Confirms full dose has been inhaled with red control window
12. If dose not completed, repeats inhalation
13. Replaces cap on device

Adapted from University of Chicago's COPD Training Documents

LABA Products

Brand Name	Generic name	Device	Color
Arcapta™	Indacaterol	Neohaler™	White/pink
Serevent®	Salmeterol	Diskus®	Teal
Striverdi®	Olodaterol	Respimat®	Yellow
Foradil®	Formoterol	No longer available in the US	

Allergy & Asthma Network - Respiratory Inhalers at a Glance 2017
GIN Guidelines 2018 Update

LAMA Products

Brand Name	Generic name	Device	Color
Incruse®	Umeclidinium	Ellipta®	Green
Seebri™	Glycopyrrolate	Neohaler®	White/orange
Spiriva®	Tiotropium bromide	Handihaler® Respimat®	Gray Pale green
Tudorza™	Acidinium bromide	Pressair™	White/green

Allergy & Asthma Network - Respiratory Inhalers at a Glance 2017
GIN Guidelines 2018 Update

LAMA/LABA Combination Products

Brand Name	Generic name	Device	Color
Anoro®	Umeclidinium/ vilanterol	Ellipta®	Red
Bevespi	Glycopyrrolate/ formoterol fumarate	Aerosphere®	White/orange cap
Stiolto™	Tiotropium bromide/ olodaterol	Respimat®	Lime green
Utibron™	Glycopyrrolate/ indacaterol	Neohaler®	White/yellow

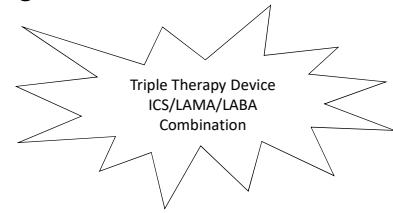
Allergy & Asthma Network - Respiratory Inhalers at a Glance 2017
GIN Guidelines 2018 Update

ICS/LABA Combination Products

Brand Name	Generic name	Device	Color
Advair®	Fluticasone propionate/salmeterol	Diskus® HFA	Purple
Breo®	Fluticasone furoate/vilanterol	Ellipta®	Light blue
Dulera®	Mometasone furoate/formoterol fumarate	MDI	Blue
Symbicort®	Budesonide/formoterol fumarate	MDI	Red

Allergy & Asthma Network - Respiratory Inhalers at a Glance 2017
GOLD Guidelines 2018 Update

Coming Soon:



Trelegy® Ellipta®
Fluticasone furoate/umeclidinium/vilanterol

GOLD Guidelines 2018 Update

Which of the following are included in recent GOLD Guidelines?

- A. COPD classification based on airway limitations alone
- B. Increased focus on symptoms and risk for exacerbations
- C. Inclusion of inhaled corticosteroids for all patients with a history of COPD exacerbations
- D. Recommendations for expanded use of roflumilast in asymptomatic patients

A 65 year old man with COPD is admitted to the internal medicine service with shortness of breath, increased dyspnea, and a cough. On a normal day, he has to stop every block to catch his breath even walking at his own speed. He has been to the emergency room three times so far this year.

How would you classify his COPD?

- A. GOLD 2
- B. GOLD 4
- C. GOLD Group D
- D. GOLD Group C

What inhaler(s) would you recommend?

- A. Spiriva HandiHaler®
- B. Proair® and Symbicort®
- C. Dulera®
- D. Anoro Ellipta®

What is the brand name for umeclidinium?

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- B. Incruse®
- C. Tudorza™
- D. Stiolto™

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- C. Neohaler™
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What class(es) of medication(s) are found in Stiolto™?

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- C. MDI
- D. Ellipta®

What class of medications is in Spiriva®?

- A. LAMA/LABA
- B. ICS/LABA
- C. LAMA only
- D. LABA only

Questions



References

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