



## Clinical Medication Therapy Review: Chronic Obstructive Pulmonary Disease (COPD) Treatment with Inhalers

**Purpose:** The NPA Medication Management Work Group acknowledges the increased need for guidance on pulmonary medications during the ongoing health crisis. The group has decided to focus on Chronic Obstructive Pulmonary Disease (COPD) due to the prevalence in the PACE population. This document provides clinical decision-making guidance for COPD and addresses considerations for administration techniques in infectious patients.

### Definitions (Abbreviations):

- **Chronic Obstructive Pulmonary Disease (COPD)**-refers to a group of diseases that cause airflow blockage and breathing-related problems. These include emphysema and chronic bronchitis. Characterized by persistent respiratory symptoms and airflow limitation. Airway abnormalities are generally caused by significant exposure to noxious particles or gases over time. Significant comorbidities may have an impact on overall morbidity and mortality.
- **Chronic Bronchitis**-long-term inflammation of the bronchi
- **Emphysema**-condition in which the alveoli are damaged
- **Spirometry**-gold standard for COPD diagnosis; the presence of a post-bronchodilator  $FEV_1/FVC < 0.70$  confirms persistent airflow limitation (see appendix A for additional information)

### Medication Classes Acronyms:

- **ICS**-Inhaled Corticosteroid
- **LABA**-Long-Acting Beta-Agonist
- **LAMA**-Long-Acting Muscarinic Antagonist
- **SABA**-Short-Acting Beta-Agonist
- **SAMA**-Short-Acting Muscarinic Antagonist

### Types of Inhalers Acronyms:

- **DPI**-Dry powder inhaler
- **MDI**-Metered dose inhaler
- **SMI**-Soft mist inhaler

**Incidence:** Based on the National Center for Health Statistics, in 2019 4.6% of adults reported a diagnosis of any type of COPD (chronic bronchitis, emphysema, or COPD). According to PACE Data Analysis Center (PDAC) of the National PACE Association, the COPD incidence (HCC 111) across all PACE sites (N=112 sites) is 30.979% based on diagnoses with dates of service from 1/1/2019-12/31/2019. The high prevalence among the PACE population speaks to the need for review of COPD treatments as an initiative.

### Classification (ICD-10): HCC 111

Chronic Obstructive Pulmonary Disease	J44.0, J44.1, J44.9
Chronic Bronchitis	J41.0, J41.1, J41.8, J42
Emphysema	J43.0, J43.1, J43.2, J43.8, J43.9, J98.2, J98.3

### Key Points and Considerations for Medication Selection:

- **Coverage**— Nebulized medications are primarily covered by Medicare Part B. There is no reimbursement for PACE plans when covered under Part B, thus it remains crucial to reserve use for acute illness and for patients that have extreme dexterity issues. Coverage under part D occurs when:
  - a nebulizer is used in a skilled nursing facility, or
  - as an inpatient in the hospital not covered by Part A stay, or
  - if a participant does not have Part A coverage.
- **Medication selection**— Newer LABAs and LAMAs have not been directly compared within class. Currently unknown whether a given patient would derive greater benefit from one agent versus another in the same class. Inhalers are available with different delivery devices and thus selection should be individualized based on participant ability.
- **Medication optimization**— Variations in medication delivery based on a patient’s ability is expected.
  - Dry powder inhalers (DPIs) have the advantage of being breath actuated and less subject to hand-breath coordination issues. DPIs require a threshold inspiratory flow, which patients with advanced COPD may be unable to generate.
  - If using MDI, which requires coordination consider adding appropriately sized spacer.
  - Nebulizer for passive administration may be required. Note though certain settings may not allow nebulization.

### Treatment Guidelines: Inhaler Pharmacologic Treatment (Generic availability in US listed in *italics* under brand)

BRAND NAME	INHALER TYPE	DRUG STRENGTH	AWP	DOSING
<b>SABA (for ACUTE treatment only)</b>				
<b>Albuterol:</b> Treatment or prevention of bronchospasm in patients with reversible obstructive airway disease, exercise-induced bronchospasm				
ProAir RespiClick, ProAir Digihaler	DPI	108 (90 Base) mcg/INH	\$75.02-\$176.00 each	2 inhalations every 4 to 6 hours as needed
ProAir HFA, Ventolin HFA, Proventil HFA, <i>Albuterol HFA*</i>	MDI	108 (90 Base) mcg/ACT	<i>\$57.03</i> -\$95.68 each	
<b>Levalbuterol:</b> Treatment or prevention of bronchospasm in patients with reversible obstructive airway disease				
Xopenex HFA <i>Levalbuterol HFA</i>	MDI	45 mcg/ACT	\$81.89 each <i>\$61.09 each</i>	2 inhalations every 4 to 6 hours as needed (maximum: 2 inhalations every 4 hours)
<b>LABA (for maintenance treatment)</b>				
<b>Salmeterol:</b> Maintenance treatment of bronchospasm associated with COPD (including emphysema and chronic bronchitis), asthma/bronchospasm, exercise-induced bronchospasm				
Serevent Diskus	DPI	50 mcg/INH	\$291.25/28-ct box \$493.36/60-ct box	1 inhalation twice daily (~12 hours apart)
<b>Olodaterol:</b> Maintenance bronchodilator treatment of airflow obstruction of patients with COPD, including chronic bronchitis and/or emphysema				
Striverdi Respimat	SMI	2.5 mcg/ACT	\$280.22 each	2 inhalations once daily (maximum: 2 inhalations per day)
<b>SAMA (acute and chronic treatment)</b>				
<b>Ipratropium:</b> Treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema				
Atrovent HFA	MDI	17 mcg/ACT	\$513.82 each	2 inhalations 4 times daily; (maximum: 12 inhalations or 204 mcg/day)

BRAND NAME	INHALER TYPE	DRUG STRENGTH	AWP	DOSING
<b>LAMA (for maintenance treatment)</b>				
<b>Acclidinium:</b> Maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema				
Tudorza Pressair	DPI	400 mcg/INH	\$342.89 each	1 inhalation twice daily
<b>Tiotropium:</b> Maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema; reduction of COPD exacerbations				
Spiriva HandiHaler	DPI	18 mcg	\$573.60/30-ct box \$1,720.81/60-ct box	Contents of 1 capsule (18 mcg) inhaled once daily using HandiHaler device
Spiriva Respimat	SMI	1.25 mcg/ACT	\$573.60 each	Asthma dosing available only
		2.5 mcg/ACT	\$573.60 each	COPD dosing: 2 inhalations once daily
<b>Umeclidinium:</b> Maintenance treatment of airflow obstruction in patients with COPD				
Incruse Ellipta	DPI	62.5 mcg/INH	\$90.06/7-ct box \$424.92/30-ct box	1 inhalation (62.5 mcg) once daily (maximum: 1 inhalation/day)
<b>ICS Maintenance and prophylactic treatment of asthma (COPD off-label)</b>				
<b>Beclomethasone</b>				
Qvar REDHALER	MDI	40 mcg/ACT	\$239.66 each	50 to 400 mcg daily as a component of dual or triple combination therapy
		80 mcg/ACT	\$320.89 each	
<b>Budesonide</b>				
Pulmicort Flexhaler	DPI	90 mcg/INH	\$230.21 each	90mcg to 400 mcg daily
		180 mcg/INH	\$308.27 each	
<b>Fluticasone</b>				
Flovent HFA	MDI	44 mcg/ACT	\$238.30 each	50 to 500 mcg/day as a component of dual or triple combination therapy
		110 mcg/ACT	\$319.02 each	
		220 mcg/ACT	\$495.53 each	
Flovent Diskus	DPI	50 mcg/blister	\$225.95/60-ct box	
		100 mcg/blister	\$238.30/60-ct box	
		250 mcg/blister	\$319.02/60-ct box	
ArmonAir Digihaler	DPI	55 mcg/INH	\$286.80 each	
		113 mcg/INH	\$286.80 each	
		232 mcg/INH	\$358.80 each	
Arnuity Ellipta	DPI	50 mcg/INH	\$220.96 each	
		100 mcg/INH	\$220.96 each	
		200 mcg/INH	\$295.81 each	
<b>Ciclesonide</b>				
Alvesco	MDI	80 mcg/ACT	\$301.88-\$329.05 each	Asthma dosing available only
		160 mcg/ACT	\$329.05 each	

BRAND NAME	INHALER TYPE	DRUG STRENGTH	AWP	DOSING
<b>ICS Maintenance and prophylactic treatment of asthma (COPD off-label) [CONTINUED]</b>				
Mometasone				
Asmanex HFA	MDI	50 mcg/ACT	\$212.87 each	Asthma dosing available only
		100 mcg/ACT	\$229.63 each	
		200 mcg/ACT	\$269.88 each	
Asmanex Twisthaler	DPI	110 mcg/INH (30 metered doses)	\$212.87 each	
		220 mcg/INH (30 metered doses)	\$229.86 each	
		220 mcg/INH (60 metered doses)	\$269.74 each	
		220 mcg/INH (120 metered doses)	\$386.52 each	
<b>SABA+SAMA</b>				
Ipratropium-Albuterol: Treatment of COPD as a secondary add-on to maintenance therapy				
Combivent Respimat	SMI	20-100 mcg/ACT	\$532.21 each	1 inhalation 4 times daily (maximum: 6 inhalations/day)
<b>LABA+LAMA</b>				
Aclidinium-Formoterol: Maintenance of airflow obstruction in COPD				
Duaklir Pressair	DPI	400-12 mcg/INH	\$1,194.00 each	1 inhalation twice daily (once in the morning and evening)
Glycopyrrolate-Formoterol: Maintenance of airflow obstruction in COPD				
Bevespi Aerosphere	MDI	9-4.8 mcg/ACT	\$474.13 each	2 inhalations twice daily
Umeclidinium-Vilanterol: Maintenance of airflow obstruction in COPD				
Anoro Ellipta	DPI	62.5-25 mcg/INH	\$521.45/60s-ct box	1 inhalation once daily
Tiotropium-Olodaterol: Maintenance of COPD, including chronic bronchitis and/or emphysema				
Stiolto Respimat	SMI	2.5-2.5 mcg/ACT	\$526.06 each	2 inhalations once daily
<b>LABA+ICS (off-label, maintenance COPD treatment as part of dual therapy)</b>				
<b>Budesonide and Formoterol</b>				
Symbicort <i>budesonide &amp; formoterol fumarate</i>	MDI	80-4.5 mcg/ACT	\$352.52-\$390.18 each	Asthma dosing available only
		160-4.5 mcg/ACT	\$402.96-\$445.99 each	2 inhalations twice daily
<b>Fluticasone and Vilanterol</b>				
Breo Ellipta	DPI	100-25 mcg/INH	\$447.19/60-ct box	Maximum: 1 inhalation [fluticasone furoate 100 mcg/vilanterol 25 mcg] once daily
		200-25 mcg/INH	\$447.19/60-ct box	Asthma dosing available only
<b>Mometasone and Formoterol</b>				
Dulera	MDI	50-5 mcg/ACT	\$373.62 each	200 mcg/ 10 mcg to 400 mcg/ 10 mcg twice daily
		100-5 mcg/ACT	\$373.62 each	
		200-5 mcg/ACT	\$373.62 each	

BRAND NAME	INHALER TYPE	DRUG STRENGTH	AWP	DOSING
<b>LABA+ICS (off-label, maintenance COPD treatment as part of dual therapy) [CONTINUED]</b>				
<b>Fluticasone and Salmeterol</b>				
Advair HFA	MDI	45-21 mcg/ACT	\$391.87 each	2 inhalations twice daily (maximum: 2 inhalations of fluticasone propionate 230 mcg/salmeterol 21 mcg twice daily)
		115-21 mcg/ACT	\$486.90 each	
		230-21 mcg/ACT	\$640.37 each	
Advair Diskus, Wixela Inhub <i>fluticasone-salmeterol diskus</i>	DPI	100-50 mcg/dose	\$357.63-\$380.46 each	1 inhalation twice daily (maximum dose: 1 inhalation of fluticasone propionate 500 mcg/salmeterol 50 mcg twice daily)
		250-50 mcg/dose	\$444.36-\$472.72 each	
		500/50 mcg/dose	\$584.42-\$621.72 each	
AirDuo Digihaler, AirDuo RespiClick <i>fluticasone-salmeterol respiclick</i>	DPI	55-14 mcg/ACT	\$119.25-\$478.80 each	1 inhalation twice daily (maximum dose: 1 inhalation of fluticasone propionate 232 mcg/salmeterol 14 mcg twice daily)
		113-14 mcg/ACT	\$119.25-\$478.80 each	
		232-14 mcg/ACT	\$119.25-\$538.80 each	
<b>LABA+LAMA+ICS (off-label, maintenance COPD treatment as part of triple therapy)</b>				
<b>Fluticasone, Umeclidinium, and Vilanterol</b>				
Trelegy Ellipta	DPI	100-62.5-25 mcg/INH	\$722.23/60-ct box	1 inhalation once daily Asthma dosing available only
		200-62.5-25 mcg/INH	\$722.23/60-ct box	
<b>Budesonide, Glycopyrrolate, and Formoterol</b>				
Breztri Aerosphere	MDI	160-9-4.8 mcg/ACT	\$708.48 each	2 inhalations twice daily (maximum dose: 2 inhalations twice daily [budesonide 640 mcg/glycopyrrolate 36 mcg/formoterol 19.2 mcg per day])

\*Albuterol HFA is generic interchange with Proventil HFA only

NOTE: Prices listed accurate as of 5/18/21. Pricing for different size boxes may change the cost per unit.

#### Administration Techniques - Key Points:

- The Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommends combination inhalation maintenance therapies for different stages of Chronic Obstructive Pulmonary Disease (COPD).
- These combinations include: long-acting  $\beta_2$ -agonists (LABA), long-acting muscarinic antagonists (LAMA), and inhaled corticosteroids (ICS).
- Poor adherence to therapy can lead to suboptimal clinical outcomes and even treatment failure.
- Single combination inhalers are available that combine LABA + LAMA, LABA + ICS, and LABA + LAMA + ICS therapies. These reduce the number of inhalers needed and doses taken per day.

### Administration Techniques - Key Points (CONTINUED):

- While there has not been robust research into the clinical benefits using single inhalers containing multiple drugs, combining inhalers has the potential to improve adherence and reduce overall costs.

<b>Patient 1 – Drug Cost/Month:</b>	
Wixela Inhub 250/50 BID -	\$444.36
<u>Spiriva 18 mcg 1 cap inhaled daily -</u>	<u>\$573.60</u>
	<b>\$1017.96</b>
<b>Patient 2 – Drug Cost/Month:</b>	
<u>Trelegy Ellipta 1 puff once daily -</u>	<b>\$722.23</b>
<i>Therapy taken at least 3 times per day is almost \$300 more/month than once daily therapy. Adherence &amp; cost is often improved by consolidating therapy.</i>	

### Drug Formulation Availability

Drugs used to treat COPD are available in a variety of formulations and devices. In the course of treatment, conversion from one formulation to another may be done to minimize certain risks (i.e., nebulization of SARS-CoV2), maximize adherence, or for cost-effectiveness considerations. The chart below can be used as a guide for alternating amongst drug classes by delivery device.

DRUG CLASS	GENERIC	NEBULIZER	MDI (compatible with spacers)	DPI	SMI
SABA	Albuterol	Albuterol, Accuneb	Ventolin, ProAir, Proventil, Albuterol HFA		
	Levalbuterol	Levalbuterol, Xopenex	Xopenex HFA		
LABA	Formoterol	Perforomist		Foradil	
	Arformoterol	Brovana			
	Salmeterol			Serevent Diskus	
	Olodaterol				Striverdi Respimat
SAMA	Ipratropium	Ipratropium	Atrovent HFA		
LAMA	Glycopyrrolate	Lonhala Magnair			
	Aclidinium			Tudorza Pressair	
	Tiotropium			Spiriva HandiHaler	Spiriva Respimat
	Umeclidinium			Incruse Ellipta	
ICS	Budesonide	Budesonide, Pulmicort Respules		Pulmicort Flexhaler	
	Mometasone		Asmanex HFA	Asmanex Twisthaler	
	Ciclesonide		Alvesco		
	Fluticasone		Flovent HFA	Flovent Diskus, ArmonAir Digihaler, Arnuity Ellipta	
	Beclomethasone		Qvar Redihaler		
SABA+SAMA	Albuterol-Ipratropium	Albuterol-Ipratropium			Combivent Respimat

## APPENDIX A- Spirometry

Spirometry is essential for the assessment of patients with suspected chronic disease of the airways. It must be performed at either the initial or a subsequent visit, if possible before and after a trial of treatment. Early confirmation or exclusion of the diagnosis of chronic airflow limitation may avoid needless trials of therapy, or delays in initiation of treatment. Spirometry confirms chronic airflow limitation but is of more limited value in distinguishing between asthma with fixed airflow obstruction, COPD and asthma-COPD overlap.

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) international COPD guidelines recommend spirometry as the gold standard for accurate and repeatable measurement of lung function. Proper diagnosis with spirometry testing can prevent both underdiagnosis, which can lead to disease progression and increased hospitalizations, and overdiagnosis, which can lead to increased health care costs and inappropriate medication use. Evidence indicates that when spirometry is used to confirm a chronic obstructive lung disease (COPD) diagnosis, more appropriate treatment is initiated; however, many primary care providers often have little formal training in spirometry and are consequently uncertain in performing and interpreting the test.

Pharmacists are well-suited to offer spirometry services to improve patient access to care and provide evidenced-based medication education and recommendations. A retrospective study by Cawley and Warning highlighted the benefits of pharmacists providing spirometry screening by preventing the delay of diagnosis, optimizing drug therapy, and optimizing teaching of delivery devices and lifestyle initiatives.<sup>1</sup> Importantly, this study also showed that pharmacists were able to perform quality spirometry testing based on the American Thoracic Society/European Respiratory guidelines.

### References:

Global Initiative for Chronic Obstructive Lung Disease. Diagnosis of Diseases of Chronic Airflow Limitation: Asthma COPD and Asthma-COPD Overlap Syndrome (ACOS) Global Initiative for Asthma Website. (Accessed 3-2021). [https://goldcopd.org/wp-content/uploads/2020/11/GOLD-REPORT-2021-v1.1-25Nov20\\_WMV.pdf](https://goldcopd.org/wp-content/uploads/2020/11/GOLD-REPORT-2021-v1.1-25Nov20_WMV.pdf)

Cawley MJ, Warning WJ. Pharmacists performing quality spirometry testing: an evidence based review. *Int J Clin Pharm.* 2015; 37:726-733.

Mueller LA, Valentino AS, Clark AD, et al. Impact of a pharmacist-provided spirometry service on access

Singh D, Agusti A, Anzueto A, Barnes PJ, Bourbeau J, Celli BR, Criner GJ, Frith P, Halpin DMG, Han M, López Varela MV, Martínez F, Montes de Oca M, Papi A, Pavord ID, Roche N, Sin DD, Stockley R, Vestbo J, Wedzicha JA, Vogelmeier C. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease: the GOLD science committee report 2019. *Eur Respir J.* 2019 May 18;53(5):1900164. doi: 10.1183/13993003.00164-2019. PMID: 30846476.

[https://www.uptodate.com/contents/management-of-refractory-chronic-obstructive-pulmonary-disease?search=copd&source=search\\_result&selectedTitle=8~150&usage\\_type=default&display\\_rank=4#H3683299604](https://www.uptodate.com/contents/management-of-refractory-chronic-obstructive-pulmonary-disease?search=copd&source=search_result&selectedTitle=8~150&usage_type=default&display_rank=4#H3683299604)  
Global Initiative for Asthma/

National Center for Health Statistics. Percentage of COPD, emphysema, or chronic bronchitis for adults aged 18 and over, United States, 2019. National Health Interview Survey. Generated interactively: May 12 2021 from [https://www.n.cdc.gov/NHISDataQueryTool/SHS\\_2019\\_ADULT3/index.html](https://www.n.cdc.gov/NHISDataQueryTool/SHS_2019_ADULT3/index.html)

Zhang S, King D, Rosen VM, Ismaila AS. Impact of Single Combination Inhaler versus Multiple Inhalers to Deliver the Same Medications for Patients with Asthma or COPD: A Systematic Literature Review. *Int J Chron Obstruct Pulmon Dis.* 2020;15:417-438. Published 2020 Feb 26. doi:10.2147/COPD.S234823