

2023 Global Initiative for Chronic Obstructive Lung Disease Report: Focus on Revised Recommendations for Inhaler Products

Kendal Pucik, PharmD Candidate and Kathy Sentena, Pharm.D., Oregon State University Drug Use Research and Management Group

Chronic Obstructive Pulmonary Disease (COPD) is a common respiratory condition, with incident rates around 10 percent worldwide in individuals aged 40 years or older.¹ It is characterized by cough, dyspnea, and airflow limitation.¹ Common risk factors include smoking, fume and dust exposure, and pulmonary or systemic infections.¹ People with COPD can have frequent office visits, hospitalization from exacerbations, and require chronic therapy, which results in high utilization of available healthcare resources.¹

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) report committee published updated guidance with recommendations for the diagnosis, management, and prevention of COPD in early 2023.² The GOLD report is updated based on new evidence identified during a standard review process that occurs twice a year.² Based on recent evidence, the GOLD Science Committee revised its recommendations on initial pharmacological treatment and follow-up pharmacological treatment for people with COPD.³ In particular, their position on the role of Long-Acting Beta Agonist (LABA) plus Long-Acting Muscarinic Antagonist (LAMA) and LABA plus Inhaled Corticosteroids (ICS) in managing COPD has been revised.³

The purpose of this newsletter is to review new evidence presented in the 2023 GOLD Report recommendations to enhance management of COPD and to describe updated COPD assessment tools. In addition, this newsletter will compare costs of recommended inhaler therapy and summarize the Oregon Health Plan (OHP) Fee-For-Service (FFS) policy for inhalers used to manage COPD.

COPD Classifications

Therapy for COPD is guided by an assessment of airflow obstruction severity, consideration of the patient's quality of life, and their risk for future events (e.g. exacerbations and hospital admissions).⁴ One common clinical tool used for assessing COPD disease severity is the modified Medical Research Council dyspnea questionnaire (mMRC).¹ This tool assesses the level of activity that causes patients to experience shortness of breath graded on a scale from 0 (dyspnea only with strenuous exercise) to 4 (too dyspneic to leave the house).¹ A second clinical tool is the COPD Assessment Test (CAT).¹ This questionnaire measures the patient's assessment of the impact of COPD on their daily life and how it changes over time.¹ It utilizes eight questions that have a value ranging from 0 (never having symptoms) to 5 (always having symptoms) which adds

to a total score.¹ A higher score indicates increased disease severity with a minimum clinically important difference defined as a change of 2 points.^{1,5} Lastly, Forced Expiratory Volume in 1 second (FEV1) as a percentage of predicted value can also be used by clinicians to measure disease severity and progression.⁴ In 2023, GOLD provided updated recommendations for how to categorize people based on COPD severity. GOLD guidelines continue to recommend that number of exacerbations, mMRC and CAT scores be used to define disease severity, but they group people into 3 levels of severity instead of 4 groups (See **Figure 1**). Members with 2 or more moderate exacerbations or at least 1 exacerbation leading to hospitalization now fall into the highest disease severity category (Group E) regardless of mMRC or CAT score; this new group is a combination of Groups C and D from previous guidelines.⁴

Figure 1. GOLD 2023 Guidance for Initial COPD Pharmacological Treatment Options⁴

≥ 2 moderate exacerbations or ≥1 leading to hospitalization	Group E: LABA + LAMA (consider LABA+LAMA+ICS if blood eosinophils ≥ 300)	
	0 or 1 moderate exacerbations (not leading to hospital admission)	Group A: bronchodilator (SABA)
	Group B: LABA+LAMA	
	mMRC 0-1, CAT < 10	mMRC ≥ 2, CAT ≥ 10

GOLD Group Classifications

For patients with a FEV1/Forced Vital Capacity (FVC) ratio less 0.7, an assessment of airflow limitation severity is based on a post-bronchodilator value of FEV1 percentage of reference value.⁴ Patients would be categorized as GOLD 1 (mild) with a FEV1 ≥ 80 percent, GOLD 2 (moderate) with a FEV1 between 50 and 79 percent, GOLD 3 (severe) with a FEV1 between 30 and 49 percent, and GOLD 4 (very severe) with a FEV1 < 30 percent.⁴

2023 GOLD Report Recommendations

The 2023 GOLD report updated previous recommendations of LAMA for patients in group B based on new evidence from a high-quality meta-analysis and randomized controlled trials (RCTs). Data from the EMAX trial provide high quality evidence that umeclidinium plus vilanterol was superior to umeclidinium monotherapy for the outcome of FEV1 at 24

weeks for patients at low exacerbation risk.^{4,6} The change from baseline in trough FEV1 at 24 weeks was 66 mL greater with umeclidinium plus vilanterol compared to umeclidinium alone (95% CI: 43 to 81, p<0.001) and 141 mL greater with umeclidinium plus vilanterol compared to salmeterol alone (95% CI: 118 to 164, p<0.001).⁶ However, it is difficult to assess the clinical meaningfulness of these results as a precise minimal clinically important difference for FEV1 has not been established.⁷ Umeclidinium plus vilanterol also demonstrated improvements in the Transition Dyspnea Index versus umeclidinium and salmeterol monotherapies at 24 weeks (versus umeclidinium: 0.37 points; 95% CI: 0.06 to 0.68; p=0.018 and versus salmeterol: 0.45 points; 95% CI: 0.15 to 0.76; p=0.004).⁶ This index measures changes in dyspnea severity from baseline and has a minimally important difference of greater than or equal to 1 unit.⁸ When compared to both salmeterol and umeclidinium monotherapy, umeclidinium plus vilanterol did show a statistically significant difference, but did not achieve thresholds for clinical meaningfulness.⁶

Mortality Benefit

Current evidence supports a reduction in mortality with pharmacotherapy and non-pharmacotherapy in COPD patients. Two RCTs, IMPACT and ETHOS, compared single inhaler triple therapy to dual long-acting bronchodilator therapy.⁴ For patients with symptoms and a history of frequent and/or severe exacerbations, both trials reported reduced mortality with triple therapy compared to dual therapy.⁴ Several RCTs have also shown reduced mortality with non-pharmacological therapy including smoking cessation, pulmonary rehabilitation, long-term oxygen therapy, noninvasive positive pressure ventilation, and lung volume reduction surgery.⁴

Additional Treatment Strategies

Most of the evidence supporting recommendations for bronchodilators in stable COPD is based on high-quality evidence from RCTs (Evidence A) or moderate quality evidence from RCTs with some limitations (Evidence B).⁴ When selecting a specific agent for a patient, considerations should be given to availability and affordability, as there are no preferred active ingredients within therapeutic classes.⁴ The recommendations for bronchodilators are listed in **Figure 2**.

Figure 2. Bronchodilators in COPD⁴

Key Points for Bronchodilators

- LABAs and LAMAs are preferred over short-acting agents except for patients with only occasional dyspnea
- When initiating treatment with long-acting bronchodilators, LABAs plus LAMAs are preferred. Patients with persistent dyspnea on a single agent should be escalated to two

The evidence supporting the recommendations for anti-inflammatory agents, specifically for ICS, is equally robust.⁴ Almost all of the recommendations are supported by publications graded as Evidence A. Important highlights for the use of anti-inflammatory agents are listed below in **Figure 3**.

Figure 3 Considerations for Treatment Selection of Anti-Inflammatory Agents⁴

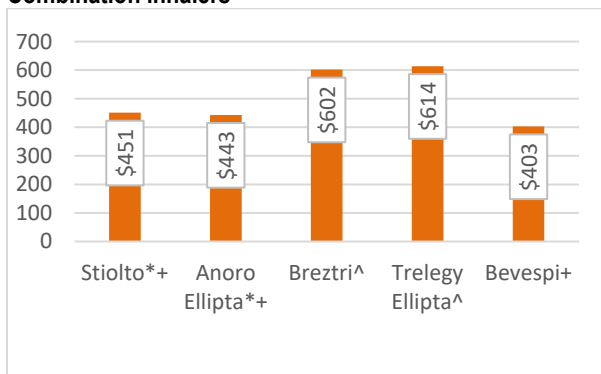
Key Points for Anti-Inflammatory Agents

- Long-term monotherapy with ICS is not recommended
- LABA plus LAMA plus ICS is preferred over LABA plus ICS therapy
- If patients with COPD have features of asthma, treatment should always contain an ICS
- If patients have a blood eosinophil count greater than or equal to 300 cells per microliter, treatment may include an ICS

Comparative Costs

Based on the 2023 GOLD report, most COPD patients should be initiated on LABA plus LAMA therapy.⁴ In addition, patients who were initiated on LABA or LAMA monotherapy and are experiencing dyspnea or exacerbations should be transitioned to combination therapy.⁴ Based on the average actual acquisition costs, dual therapy inhalers cost more than single agent products; however, the cost is lower than two separate monotherapy inhalers. The average acquisition costs for long-acting agents are listed in **Figure 4**. Also, combination inhalers may also improve adherence as non-adherence rates to COPD medication are estimated to be between 22 and 93 percent (depending on the definition of adherence used).⁹ Overall, therapy selection should be patient specific, considering several factors including disease burden, patient lifestyle, and comparative costs.

Figure 4. Comparative Monthly Cost of Long-Acting Agents Combination inhalers



* OHP FFS Preferred Agent
 +LABA/LAMA dual therapy inhaler
 ^LABA/LAMA/ICS triple therapy inhaler
 **Prices based on 1 inhaler from Myers and Stauffer. Accessed July 24, 2023.

OHP FFS Policy Guidance

Preferred therapies for FFS members are based on effectiveness, safety and cost considerations (Figure 5).

Figure 5. Preferred Treatment Options for Inhaled COPD Treatment

OHP FFS Preferred COPD Inhalers

- SAMA: Atrovent or Combivent,
- LABA: Serevent
- LAMA: Spiriva or Incruse Ellipta
- LABA + LAMA: Stiolto or Anoro Ellipta

Conclusion

The 2023 Gold report provides updated recommendations for initial therapy options in patients with COPD.¹⁰ These recommendations support the use of LABA plus LAMA combination therapy over monotherapy.¹⁰ The updated recommendations provide a simplified treatment algorithm that will hopefully benefit providers and patients.¹⁰

Peer Reviewed By: Tracy Klein, PhD, ARNP, FAANP, FRE, FAAN, Associate Professor, College of Nursing Washington State University Vancouver and Ucheoma Nwizu, PharmD., BCACP, Med., Clinical Pharmacy Manager Neighborhood Health Center, Milwaukie, Oregon

References:

- King Han MD, M; Martinez, F. Chronic obstructive pulmonary disease: Diagnosis and staging. May 31, 2023. Accessed July 19, 2023.
- Global Initiative for Chronic Obstructive Lung Disease. Accessed July 3, 2023. <https://goldcopd.org/>
- GOLD 2023 Key Changes Summary. Accessed July 3, 2023. <https://goldcopd.org/wp-content/uploads/2022/12/KEY-CHANGES-GOLD-2023-2.pdf>
- 2023 Gold Report. Accessed July 3, 2023. <https://goldcopd.org/2023-gold-report-2/>
- Kon SS, Canavan JL, Jones SE, et al. Minimum clinically important difference for the COPD Assessment Test: a prospective analysis. *Lancet Respir Med.* Mar 2014;2(3):195-203. doi:10.1016/s2213-2600(14)70001-3
- Maltais F, Bjermer L, Kerwin EM, et al. Efficacy of umeclidinium/vilanterol versus umeclidinium and salmeterol monotherapies in symptomatic patients with COPD not receiving inhaled corticosteroids: the EMAX randomised trial. *Respir Res.* Oct 30 2019;20(1):238. doi:10.1186/s12931-019-1193-9
- Donohue JF. Minimal clinically important differences in COPD lung function. *Copd.* Mar 2005;2(1):111-24. doi:10.1081/copd-200053377
- Baseline Dyspnea Index (BDI) & Transition Dyspnea Index (TDI). American Thoracic Society. Accessed July 25, 2023. <https://www.thoracic.org/members/assemblies/assemblies/srn/questionnaires/bdi-tdi.php>
- Bhattarai B, Walpola R, Mey A, Anoopkumar-Dukie S, Khan S. Barriers and Strategies for Improving Medication Adherence Among People Living With COPD: A Systematic Review. *Respir Care.* Nov 2020;65(11):1738-1750. doi:10.4187/respcare.07355
- 2022 GOLD Report. Accessed July 3, 2023. https://goldcopd.org/wp-content/uploads/2021/12/GOLD-REPORT-2022-v1.1-22Nov2021_WMV.pdf