COPD Pharmacotherapy Review

Based on the 2025 GOLD Report (Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease)

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Abbreviations

eos Blood eosinophil count (cells/mcL)
ICS Inhaled corticosteroid
LABA Long-acting beta-agonist
LAMA Long-acting muscarinic antagonist
SABA Short-acting beta-agonist
SAMA Short-acting muscarinic antagonist

COPD Treatment Goals

Stable COPD	COPD Exacerbations
• **Improve** symptoms, exercise tolerance, health	• **Minimize** the effects of the exacerbation
• **Reduce risks of** disease progression, exacerbations, death	• **Prevent** future exacerbations

Initiation of Pharmacotherapy in Stable COPD

Select initial pharmacotherapy based on current symptoms and exacerbation history

Note
- If combination therapy is chosen, consider **single-inhaler options** for patient convenience
- Short-acting bronchodilators should be prescribed to all patients for immediate symptom relief

Exacerbations

≥2 moderate exacerbations OR ≥1 resulting in hospital admission

E

LABA + LAMA

- If eos ≥300, consider LABA + LAMA + **ICS**

≤1 moderate exacerbations not resulting in hospital admission

A

Bronchodilator
(LABA, LAMA, SABA, or SAMA)

- Either long- or short-acting, but **long-acting is generally preferred** unless very occasional dyspnea

CAT <10, mMRC 0-1

B

LABA + LAMA

- If LABA + LAMA combo is not appropriate, **choose either** based on the patient's perceived symptom relief

CAT ≥10, mMRC ≥2

Symptoms

CAT: COPD Assessment Test
mMRC: Modified Medical Research Council dyspnea scale

Adapted from Figure 3.7 of the 2025 GOLD Report

Pharmacotherapy Key Points

General Notes on Inhaled Medications

- **Individualize** inhaler choice (e.g., cost, ability to use, efficacy)
- Assess inhaler technique and adherence prior to therapy modification

Bronchodilators - First-Line for COPD

- **Long-acting** agents (LABA, LAMA) are **preferred** over short-acting (SABA, SAMA), except in those with only **occasional dyspnea** and when **immediate relief** is needed in those on long-acting maintenance therapy
- **Combination** of LAMA+LABA is more effective at improving symptoms and lung function than monotherapy; patients not managed on a single long-acting bronchodilator should be **escalated** to dual therapy
- LAMAs provide greater exacerbation risk reduction than LABAs
- Combination of SABA+SAMA is more effective than either alone
- **Inhaled** bronchodilators are recommended over oral bronchodilators

Inhaled Corticosteroids (ICS) - Main Anti-Inflammatory Therapy

- ICS **monotherapy** has **not** shown long-term benefit in COPD treatment
- Can be **added** to LABA+LAMA in patients with exacerbation history (especially if recurrent or has led to hospitalization) or **eos ≥100**
  - ICS **should** be included if features of **asthma** are present
- ICS+LABA+LAMA has proven mortality benefit versus LABA+LAMA in those with symptomatic COPD and history of exacerbations
- ICS+LABA **not** encouraged for COPD; if ICS is indicated, use **triple regimen**
- Main safety concern is **pneumonia**; not recommended in patients with history of **recurrent pneumonia** or **mycobacterial infection**

Others - PDE Inhibitors, Dupilumab, Antibiotics

- **Roflumilast** (PDE-4 inhibitor) reduces **exacerbations** and improves **lung function** in those with **severe to very severe airflow limitation**, **chronic bronchitis**, and **exacerbations**
  - Consider adding to LABA+LAMA (+/- ICS) for these patients
- **Ensifentrine** (PDE-3 and -4 inhibitor) improves lung function and dyspnea
  - Consider adding to LABA+LAMA in patients with **dyspnea**
- **Dupilumab** (IL-4 and IL-13 inhibitor) reduces exacerbations and improves lung function in patients with **chronic bronchitis**, history of **exacerbations** despite LABA+LAMA+ICS therapy, and **eos ≥300**
  - Consider adding to triple therapy for these patients if exacerbations occur
- In those with exacerbations despite appropriate therapy, **macrolides** (e.g., azithromycin) may be considered (especially in **former smokers**)

Follow-Up Pharmacotherapy Management in Stable COPD

COPD management is an individualized, continuous cycle of assessment and treatment adjustment

Is COPD well managed?

Review:
- Symptoms (e.g., dyspnea)
- Exacerbations

Assess:
- Inhaler technique & adherence
- Non-pharmacological interventions

Adjust:
- Consider escalation/de-escalation
- Switch device or medications

No →

If Yes: Continue current therapy

Adapted from Figures 3.8 and 3.9 of the 2025 GOLD Report

Inhalers Chart + Administration Guides

Primary Issue?*

Dyspnea

LAMA or LABA

↓

LAMA + LABA**

↓

- Consider switching inhaler or medication
- Optimize non-pharmacological interventions
- Assess and address other causes of symptoms
- Consider adding **ensifentrine**

Exacerbations

LAMA or LABA

↓

LAMA + LABA**

← eos <300 / eos ≥300 ↓

eos ≥100 / eos <100 ↓

LAMA + LABA + ICS**
(Consider **de-escalating** to LAMA + LABA if ICS is not tolerated or not effective)

→ If eos ≥300 ↓ Consider adding **dupilumab** if symptoms of **chronic bronchitis** are present

Consider adding:
- **Roflumilast** if FEV1 <50% + chronic bronchitis
- **Azithromycin**, preferentially in former smokers

Although LABA+ICS is not preferred in treatment of COPD without features of asthma, if the patient has already been on LABA+ICS and is well managed, the current therapy **may** be continued (or consider switching to LABA+LAMA if no relevant exacerbation history).
- If **exacerbations** occur, escalate to LABA+LAMA+ICS (if eos ≥100) **or** switch to LABA+LAMA (if eos <100)
- If major symptoms are present, decide based on previous response to ICS:
  - If no relevant history of exacerbation, consider switching to LABA+LAMA
  - If history of positive response to ICS in previous exacerbations, consider escalating to LABA+LAMA+ICS

*If **both** dyspnea and exacerbation must be addressed, **use the exacerbation pathway**
**For patients on LAMA+LABA or LAMA+LABA+ICS, single-inhaler options should be considered for convenience

Pharmacotherapy Management of Acute Exacerbations*

*Non-life-threatening

Initial Treatment: SABA (with or without SAMA) →

- Initiate maintenance with **long-acting bronchodilators** as soon as stable
  - Consider adding **ICS** to LAMA+LABA if frequent exacerbations with ↑ eos
- If severe exacerbation, consider **systemic corticosteroids** (duration: generally **≤5 days**)
- If indicated (e.g., signs of bacterial infection), give **antibiotics** (duration: generally **5-7 days**)

Reference: Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2025 Report)

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