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Focus on COPD – Part 2: Pharmacological Treatment Options

- by Ellie Kang and Allen Lefkovitz

Proper management of chronic obstructive pulmonary disease (COPD), though not curative, may slow its progression. Unfortunately, it is estimated that an average of 60% of patients with COPD do not adhere to their prescribed therapy, thereby limiting its benefits.

Over the past two years, significant updates have been made to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. As discussed in the July 2018 Focus article on COPD, the GOLD guidelines outline 4 different patient groups (A, B, C, and D). These patient groups, as with previous GOLD guidelines, serve as the foundation for the GOLD treatment algorithms.

Initial treatment per the 2018 GOLD guidelines for a majority of the patient groups consists of stand-alone or combinations of short-acting ß-2 agonists (SABA), short-acting muscarinic antagonists (SAMA), long-acting ß-2 agonists (LABA), or long-acting muscarinic antagonists (LAMA). Table 1 provides a summary of the specific recommendations made in the 2018 GOLD guidelines.

Although still within the treatment pathway, combinations with inhaled corticosteroids (ICS) are no longer recommended as initial therapy for Group C or D patients. ICS have been associated with an increased risk for developing pneumonia in some individuals. Therefore, ICS combinations are reserved for therapy when symptoms continue to progress. Another change includes reserving Daliresp (roflumilast) for only Group D patients with an FEV_1 < 50% and a diagnosis of chronic bronchitis.

Table 1. Pharmacological Management of COPD (GOLD 2018)

Patient Group	Recommended Initial Therapy	Suggested Progression of Therapy
A	Short- or long-acting bronchodilator	Alternative class of bronchodilator
B	LAMA or LABA	LAMA and LABA†
C	LAMA	• LAMA and LABA† • LABA and ICS
D	LAMA and LABA	• LAMA and LABA and ICS† • LABA and ICS *if FEV_1 < 50% and patient has chronic bronchitis: consider adding roflumilast; if former smoker: consider adding macrolide (e.g., azithromycin)*

LABA = long-acting beta-agonist (e.g., formoterol, salmeterol)
LAMA = long-acting muscarinic antagonist (e.g., glycopyrrolate, tiotropium)
ICS = inhaled corticosteroid (e.g., budesonide, fluticasone)
† listed as "Preferred treatment" pathway in GOLD 2018

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While combinations of therapies often become necessary, evidence-based statements within GOLD 2018 include the following:

- "Inhaled bronchodilators in COPD are central to symptom management and commonly given on a regular basis to prevent or reduce symptoms"
- "Combinations of SABA and SAMA are superior compared to either medication alone in improving FEV_1 and symptoms"
- "LABAs and LAMAs significantly improve lung function, dyspnea, health status, and reduce exacerbation rates"
- "LAMAs have a greater effect on exacerbation reduction compared with LABAs and decrease hospitalizations"

Other Therapies Not Recommended in GOLD 2018

Another major change noted was the removal of theophylline and acetylcysteine as "other possible treatments". In prior GOLD guidelines, theophylline was listed under "other possible treatments" in all patient groups; acetylcysteine was reserved for patient group D. Although removed from the treatment pathways, GOLD 2018 does still state that "Theophylline exerts a small bronchodilator effect in stable COPD and that is associated with modest symptomatic benefits."

Other therapies have been utilized in the management of COPD, but the GOLD guidelines **do not** currently recommend the following for routine use:

Alpha-1 antitrypsin augmentation therapy	Shown to potentially slow down the progression of emphysema in those with alpha-1 antitrypsin deficiency. There is no evidence to support their use in other COPD patients.
Antibiotics	Shown efficacy for the acute treatment of infectious exacerbations of COPD. With the exception of macrolide antibiotics (e.g., azithromycin), continuous use of an antibiotic, in general, has no effect on the frequency of exacerbations. Even with macrolide antibiotics, there is no efficacy or safety data beyond one year of treatment, but use was associated with increased risk of bacterial resistance. With antimicrobial stewardship being such an important topic, it is in the best interest of the patient to avoid unnecessary use of antibiotics, in order to reduce antibiotic resistance complications.
Antitussives (e.g., dextromethorphan)	Shown potential benefit in some individuals with viscous sputum, but given the protective nature of coughing, antitussives may actually mask the progression of the disease. The 2018 GOLD guidelines limit their discussion on antitussives to the statement that their role in patients with COPD is "inconclusive".
Leukotriene modifiers (e.g., montelukast)	Not approved for COPD and are inadequately tested to recommend their use.
Systemic corticosteroids (e.g., prednisone)	May be used for acute exacerbations. However, long-term use lacks evidence of benefit and carries significant risks (e.g., osteoporosis, hyperglycemia).
Vasodilators (e.g., sildenafil, tadalafil)	have not demonstrated significant improvement in outcomes and potentially may increase pulmonary artery pressure and worsen oxygenation.

The 2018 GOLD Guidelines are avaiable for free at: https://goldcopd.org/gold-reports/

NEW Generic Medications

- by Allen Lefkovitz

Generic Name	Brand Name	Date Generic Available
Hydroxyprogesterone Caproate 250 mg/mL Injection	Makena® Injection	7/2/18
Buprenorphine/Naloxone 8 mg/2 mg Sublingual Film	Suboxone® Sublingual Film	6/22/18

NEW Drugs

Olumiant® Tablets

- by Dave Pregizer

Brand Name (Generic Name)	**Olumiant [O-loo-me-ant] (baricitinib) [bar-i-SYE-ti-nib]**
How Supplied	2 mg tablets
Therapeutic Class	Janus kinase (JAK) inhibitor
Approved Indication	Treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more TNF antagonist therapies (e.g., Enbrel). Combination with other JAK inhibitors, biologic DMARDs, or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.
Usual Dosing	2 mg once daily. May be used as monotherapy or in combination with methotrexate or other DMARDs. Avoid initiation or interrupt use with hemoglobin < 8 g/dL or with an absolute lymphocyte count < 500 cells/mm^3 or absolute neutrophil count < 1000 cells/mm^3.
Select Drug Interactions	Not recommended for use with strong Organic Anion Transporter 3 (OAT3) inhibitors (e.g., probenecid) due to increased baricitinib exposure
Most Common Side Effects	Upper respiratory tract infections, nausea, herpes simplex, and herpes zoster
Miscellaneous	Boxed Warning for serious infections (e.g., tuberculosis, invasive fungal infections), malignancy, and thrombosis. Not recommended with severe hepatic impairment or with moderate or severe renal impairment.
Website	Olumiant.com

DMARDs: disease-modifying antirheumatic drugs

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Zemdri® Injection

Brand Name (Generic Name)	**Zemdri [Zem-dri] (plazomicin) [pla-zoe-MYE-sin]**
How Supplied	500 mg/10 mL (50 mg/mL) single-dose, 10 mL vials
Therapeutic Class	Aminoglycoside antibacterial
Approved Indication	Treatment of adults with complicated urinary tract infections (cUTI) including pyelonephritis. Reserve use for patients with limited or no alternative treatment options.
Usual Dosing	15 mg/kg every 24 hours by intravenous infusion over 30 minutes for 4 to 7 days. Assess creatinine clearance prior to initiating therapy and daily during therapy. See full Prescribing Information for recommended initial dosing and subsequent dosage adjustments based on changes in renal function or therapeutic drug monitoring.
Select Drug Interactions	Avoid concomitant use with other potentially nephrotoxic and ototoxic agents
Most Common Side Effects	Reduced renal function, high or low blood pressure, headache, diarrhea, nausea, vomiting
Miscellaneous	Boxed warning for nephrotoxicity, ototoxicity, neuromuscular blockade and fetal harm. Dilute in 0.9% Sodium Chloride or Lactated Ringer's injection for a final volume of 50 mL.
Website	zemdri.com

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