INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: *COPD Guidelines Review*
-August 2026-

Background:
The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) provided a drug class review of Chronic Obstructive Pulmonary Disease (COPD) agents. Currently, medications listed on the IHS National Core Formulary that are relevant to the treatment of COPD include albuterol, ipratropium, tiotropium, azithromycin, and umeclidinium/vilanterol. Following review and analysis, the NPTC voted to **add budesonide, glycopyrrolate, and formoterol fumarate** (triple combination, single inhaler) to the National Core Formulary.

Discussion:
Chronic Obstructive Pulmonary Disease is a heterogeneous pulmonary condition characterized by persistent airflow obstruction despite use of pharmaceutical bronchodilators, with pathophysiologic features including emphysema, chronic bronchitis, and/or small airways disease. Pathologic structural changes in the airways, lung parenchyma, and pulmonary vasculature result in persistent airflow obstruction, which proceeds to increased residual lung volume, non-uniform distribution of ventilation, and ultimately ventilation-perfusion mismatch.[1] Risk factors for COPD include cigarette smoking, vaping or e-cigarette use, occupational exposures, smoke due to biomass combustion, pollution exposure, chronic infections, developmental factors such as prematurity at birth, and alpha-1 anti-trypsin deficiency. Prevalence of COPD in the United States in 2024 was 4.2% in the general population and 6.6% in the American Indian/Alaska Native (AI/AN) population.[2] COPD is twice as common among people with a low family income and among those residing outside of a major metropolitan area.

The diagnosis of COPD is based on a combination of clinical examination and spirometry measurement (FEV1 [Forced Expiratory Volume], FVC [Forced Vital Capacity], FEV1/FVC ratio). Symptoms of exacerbation include increased respiratory symptoms (dyspnea, cough), sputum or sputum purulence, and a need for PRN rescue medications. COPD exacerbations negatively impact quality of life, accelerate disease progression, promote hospitalization, and increase risk of death. Management of symptoms and prevention of exacerbations is therefore the focus of most COPD therapies. Correct diagnosis and classification by severity are essential for determining appropriate treatment.

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) has developed diagnostic criteria and treatment guidelines for COPD.[1] Diagnosis is based on clinical evaluation and post-bronchodilator spirometry demonstrating an FEV1/FVC < 0.7, with measurement of blood eosinophil levels as a tool for assessing degree of type 2 inflammation involved. Severity of disease state is characterized by airflow limitation, by symptoms using the Modified Medical Research Council (mMRC) Dyspnea and Chronic Airway Assessment Test (CAAT) surveys, and by frequency of exacerbations. After diagnosis, individuals are categorized into three groups (A, B, E) with recommended pharmaceutical treatments. Blood eosinophil counts assist in the decision to add an inhaled corticosteroid to treatment regimens.

GOLD ASSESSMENT CATEGORY	SYMPTOMS (mMRC and CAAT)	EXACERBATIONS (PAST YEAR)
Category A	mMRC 0-1; CAAT < 10	No moderate or severe exacerbations
Category B	mMRC ≥ 2; CAAT ≥ 10	No moderate or severe exacerbations
Category E	Any mMRC score, Any CAAT score	≥ 1 moderate or severe exacerbation

Treatment recommendation for Category A patients includes use of a bronchodilator. Treatment recommendation for Category B patients includes use of an inhaled dual long-acting muscarinic antagonist (LAMA) and a long-acting beta agonist (LABA). Treatment recommendation for Category E patients involves use of a LAMA+LABA and consideration of use of an inhaled corticosteroid (ICS) as “triple therapy” based on blood eosinophils levels, frequency of moderate or severe exacerbations, and/or hospitalization for an exacerbation. An ICS should be used in individuals with concomitant asthma regardless of GOLD assessment category. Further exacerbations despite use of triple therapy (or LAMA+LABA without type 2 inflammation) should prompt consideration for use of a phosphodiesterase-4 inhibitor (e.g., roflumilast), macrolide (e.g., azithromycin) or biologic (e.g., dupilumab or mepolizumab) in the appropriate clinical context.

Additional guidelines reviewed were those published by the British National Institute for Health and Care Excellence and the Canadian Thoracic Society.[3,4] While some variation exists in guidelines, key management recommendations within all involve the use of LAMA+LABA for moderate or severe disease and consideration of ICS with exacerbations.

Regarding the use of eosinophils as a marker of type 2 inflammation and to guide use of an ICS, the GOLD guidelines cite a post-hoc analysis of three randomized trials comparing use of a LABA+ICS to a LABA in patients with COPD.[5] The analysis found that exacerbation rates increased as eosinophil counts increased in patients with COPD using formoterol alone. However, rates remained stable in patients treated with LABA+ICS therapy, despite increasing eosinophils. There was a reduction in exacerbations with budesonide-formoterol compared with formoterol, beginning at an eosinophil level of more than 100 cells/L (Rate Ratio [RR] 0.75, 95% CI 0.57-0.99, p=0.015) and increasing in benefit with increases in eosinophil counts.

Regarding the use of single-inhaler triple therapy for advancing symptoms and moderate or severe exacerbations, the GOLD guidelines cite two large randomized clinical trials known as the IMPACT and ETHOS trials.[6,7] The IMPACT trial compared use of fluticasone/umeclidinium/vilanterol to fluticasone/vilanterol and to umeclidinium/vilanterol. It found a 15% reduction in exacerbations per year with triple therapy compared to LABA+ICS therapy (RR 0.85, 95% CI 0.80-0.90, p<0.001), and a 25% reduction compared to LAMA+LABA (RR 0.75, 95% CI 0.70-0.81, p<0.001). The ETHOS trial compared use of lower and higher doses of budesonide, glycopyrrolate and formoterol to budesonide/formoterol and to glycopyrrolate/formoterol. At both high and low doses, triple therapy reduced exacerbations compared to LAMA+LABA (high dose RR 0.76, 95% CI 0.69-0.83, p<0.001; low dose RR 0.75, 95% CI 0.69-0.83, p<0.001) and compared to LABA+ICS (high dose RR 0.87, 95% CI 0.79-0.95, p=0.003; low dose RR 0.86, 95% CI 0.079-0.95, p=0.002). Both trials also found that lung function, symptoms, and health status measures improved with use of triple therapy. However, both studies found an increased frequency of pneumonia in patients treated with an ICS.

Emerging evidence has additionally supported better adherence to a single inhaler with combined medication as therapy compared to use of multiple inhalers for therapy.[8]

Non-pharmacologic treatment strategies are noted in the GOLD guidelines and include risk reduction (e.g., smoking cessation, education, vaccination), pulmonary rehabilitation, long-term oxygen use, non-invasive ventilation, surgical therapies, and palliative therapies.

Findings:

Updates from professional society guidelines focused on COPD diagnosis and management continue to emphasize the use of both short-acting and long-acting inhaled bronchodilators as a mainstay of treatment. Since the prior 2019 IHS formulary brief on COPD, the GOLD guidelines have consolidated their assessment categories used for initial pharmaceutical treatment and subsequent adjustment of treatment. Similarly, these guidelines now point to the use of blood eosinophil measurements as a clinical support tool to determine the use of an ICS in COPD without concomitant asthma, among other criteria. With advancement of symptoms or continued exacerbations, the guidelines support consideration for the use of phosphodiesterase-4 inhibitors, macrolides, and/or biologics.

In the United States, COPD disproportionately affects the AI/AN population in comparison to the general population. The addition of single-inhaler triple therapy to the National Core Formulary in the form of budesonide, glycopyrrolate and formoterol fumarate provides an opportunity to ensure appropriate initial therapy, or stepwise increased therapy from a LAMA+LABA, supporting availability across the agency for patients with advancing COPD who meet guideline recommendations and who may benefit from use of an ICS as part of their treatment regimen.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov . For more information about the NPTC, please visit the NPTC website.

References:

1. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of COPD: 2026 Report. 2026
2. National Center for Health Statistics. Summary health statistics for U.S. adults, 2024. NHIS-Adult Summary Health Statistics. 2024.
3. National Institute for Health and Care Excellence. Chronic obstructive pulmonary disease in over 16s: diagnosis and management. 2019.
4. Bourbeau J, Bhutani M, Hernandez P, et al. 2023 Canadian Thoracic Society guideline on pharmacotherapy in patients with stable COPD. *Chest.* 2023; 164(5):1159-83.
5. Bafadhel M, Peterson S, De Blas MA, et al. Predictors of exacerbation risk and response to budesonide in patients with chronic obstructive pulmonary disease: a post-hoc analysis of three randomised trials. Lancet Respir Med. 2018; 6(2):117-26.
6. Lipson D, Barnhart F, Brealey N, et al. Once-Daily Single-Inhaler Triple versus Dual Therapy in Patients with COPD. NEJM. 2018;378(18):1671-80.
7. Rabe KF, Martinez FJ, Ferguson GT, et al. Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD. NEJM. 2020; 383(1):35-48.
8. Halpin DMG, Rothnie KJ, Banks V, et al. Comparative adherence and persistence of single- and multiple-Inhaler triple therapies among patients with chronic obstructive pulmonary disease in an English real-world primary care setting. Int J Chron Obstruct Pulmon Dis. 2022; 17:2417-29.