Mepolizumab INJ (NUCALA) for Chronic Obstructive Pulmonary Disease (COPD)
Criteria for Use
October 2025

VA Pharmacy Benefits Management Services and National Formulary Committee

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

See the VA National Formulary Committee Monograph on this drug at the *PBM INTRAnet* site for further information.

Exclusion Criteria

If any of the following are selected, the patient will NOT meet criteria for Mepolizumab.

- ☐ Untreated acute bronchospasm or acute exacerbation of chronic obstructive pulmonary disease (COPD)
- ☐ Untreated parasitic (helminth) infection (treat the infection prior to initiating mepolizumab)
- ☐ Concurrent use with therapeutic biologics unless potential benefit-risk favors use

Inclusion Criteria

All the following criteria must be selected to meet criteria.

- ☐ Provider is a VA or VA Community Care pulmonologist or designated expert
- ☐ Moderate to severe COPD (e.g., post-bronchodilator FEV_1 30-70% predicted and FEV_1/FVC <0.7, confirmed by pulmonary function testing) ^1
- ☐ Blood eosinophils 300 cells/µL or greater obtained prior to treatment (e.g., within the 3 months prior)
- ☐ Signs or symptoms of chronic bronchitis (chronic productive cough) for at least 3 months during the past year
- ☐ Receiving concurrent triple inhaled therapy with a long-acting beta-agonist (LABA) AND a long-acting anticholinergic (LAMA) AND an inhaled corticosteroid (unless inhaled corticosteroid is contraindicated) for at least 3 months
- ☐ Had at least 2 moderate COPD exacerbations (requiring systemic steroids and/or antibiotics) or at least 1 severe COPD exacerbation (requiring hospitalization) in the previous 12 months
- ☐ Inadequate symptom control (e.g., mMRC dyspnea scale score $\geq$ 2) or impaired health status (e.g., CAT score $\geq$ 15) ^2
- ☐ Patient is unable to tolerate or had an inadequate response to a (6-month) trial of roflumilast and to a (6-month) trial of azithromycin, unless not clinically appropriate for either agent (e.g., risk outweighs benefit) ^3-5
- ☐ Adherent to COPD medications as evidenced by a review of prescription refill history
- ☐ Patient demonstrated correct inhaler technique (documented in chart) ^6

^1 If the patient has a concomitant diagnosis of asthma, refer to the benralizumab CFU in patients with asthma.

^2 mMRC=Modified Medical Research Council dyspnea scale; https://www.pcrs-uk.org/sites/default/files/resources/MRC-Score.pdf; CAT=COPD assessment test.

^3 Roflumilast can reduce exacerbations in patients with FEV_1 <50% predicted and chronic bronchitis. Gastrointestinal adverse events can be minimized with titration. Psychiatric effects including insomnia, anxiety, depression and suicidal thoughts may occur and patients should be informed. Weigh the benefit/risk in patients with a history of depression and/or suicidal thoughts or behavior. Combination with strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, etc.) is not recommended. Concomitant use with CYP3A4 and/or CYP1A2 inhibitors may increase risk for adverse events. Do not use in patients with moderate to severe liver impairment (e.g., Child-Pugh B or C).

^4 Azithromycin can reduce exacerbations in patients with FEV_1 <50% predicted and an exacerbation in the past year. Adverse events include prolonged QTc and hearing loss. Weigh benefit/risk in patients receiving multiple QT prolonging drugs, baseline hearing loss and concern for atypical mycobacterial infection.

^5 A trial of both listed agents is not required, if not clinically appropriate.

^6 Proper use of the inhaled device should be confirmed. If the patient is unable to use their inhaled device properly, consider changing to an alternative device (DPI, SMI, MDI). If a switch is made, reassess, and confirm ability to use device properly.

Additional guidance:

Patient is non-smoking or, if not, he/she is enrolled in a quit smoking program or on medications to assist with smoking cessation. Current smokers may be considered if unable or refuse to quit.

Recommend addressing modifiable environmental triggers for Type 2 inflammation, if not already done.

Additional Inclusion Criteria: Select if applicable

Select if applicable.

☐ For females who can become pregnant: Counseling provided on potential risks vs benefits of treatment and the use of effective contraception during therapy.

Other Justification

☐ Patient with a diagnosis of hypereosinophilic syndrome (HES) to reduce eosinophilia and minimize exposure to glucocorticoids prescribed by a specialty provider (e.g., Hematologist) experienced in managing HES.

☐ Patient with non-severe active eosinophilic granulomatosis with polyangiitis (EGPA) to induce remission, prevent relapse and to minimize exposure to glucocorticoids and prescribed by a specialty provider experienced in managing EGPA and with an inadequate response to benralizumab.

Supplemental Information

- The Global Initiative for Chronic Obstructive Lung Disease, or GOLD, guidelines recommend considering roflumilast or azithromycin in patients that are on dual (eosinophils <100 cells/microliter) or triple inhaler therapy (eosinophils >100 cells/microliter) and continue to have exacerbations despite adherence with inhaled therapy and confirmed ability to use inhalers properly. Despite general guidance for use (e.g., roflumilast in patients with FEV1 <50% prediction and with chronic bronchitis or azithromycin, preferentially in former smokers), there is no clearer guidance directing the optimal choice between the two agents for reducing exacerbation risk. There is an ongoing multicenter, noninferiority, comparative effectiveness study (RELIANCE) comparing azithromycin (250 mg daily, 500 mg three times weekly or alternate regimen) to roflumilast (500 mg daily or alternate regimen) in patients with COPD and chronic bronchitis who were hospitalized in the past year. The study is estimated to be completed in 2026.
- In patients with COPD receiving triple inhaled therapy (LAMA+LABA+ICS), eosinophils $\geq$ 300 cells/microL and chronic bronchitis who continue to have exacerbations despite maximal therapy, GOLD recommends considering addition of dupilumab. FDA approval of mepolizumab for COPD with an eosinophilic phenotype was not granted until May 2025 but place in therapy is expected to be similar to dupilumab.
- For patients with recurrent exacerbations despite maximized inhaled therapy, UpToDate suggests roflumilast, azithromycin, dupilumab or mepolizumab as options. The choice between the agents is largely based upon patient and disease characteristics from populations studied in clinical trials. For example, eosinophilic phenotype is required for both dupilumab and mepolizumab, presence of chronic bronchitis and FEV1 <50% predicted for roflumilast and more broadly for azithromycin in patients with bronchiectasis or recurrent bacterial infections but preferentially in former smokers. Additionally, potential for adverse events (ADE) should also be considered in the selection including gastrointestinal ADE and risk for psychiatric effects including insomnia, anxiety, depression and suicidal thoughts for roflumilast, long corrected QT interval (QTc) and hearing loss with azithromycin and injection site and hypersensitivity reactions for dupilumab and mepolizumab. None of the agents have been compared directly.

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