Mepolizumab (NUCALA) in Chronic Obstructive Pulmonary Disease (COPD)
National Drug Mini-Monograph
October 2025

VA Pharmacy Benefits Management Services and National Formulary Committee

The purpose of VA National Formulary Committee drug monographs is to provide a focused drug review for making formulary decisions. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA APPROVAL INFORMATION

Description / MOA	Humanized monoclonal antibody which binds to interleukin-5, leading to a reduction in eosinophils.
Indication Under Review[1]	Add-on maintenance therapy in adults with inadequately controlled chronic obstructive pulmonary disease (COPD) with an eosinophil phenotype.
Dosage Regimen	100 mg SQ every 4 weeks
Dosage Forms Under Review	100 mg injection single dose vial, 100 mg single dose prefilled syringe and prefilled autoinjector.

EFFICACY CONSIDERATIONS

Trial	**MATINEE Study[2]**
Design	R, DB, MC, PC
Population	Adults with COPD, FEV_1/FVC <0.7 before and after albuterol; FEV_1 ≥ 20% but not >80% predicted after albuterol; ≥ 2 moderate exacerbations or ≥ 1 severe over the prior 12 months; receiving triple inhaler therapy with ICS/LABA/LAMA for at least 3 months before screening and eosinophils ≥300 cells/microL. *Patients with asthma were excluded.*
Intervention	Mepolizumab 100 mg SQ every 4 weeks for 52-104 weeks
Comparator	Placebo (PBO) SQ every 4 weeks for 52-104 weeks

Results

Outcome Measures	Mepolizumab (n=403)	Placebo (n=401)
Primary: Annualized rate moderate or severe exacerbation-events/yr (95% CI)	0.8 (0.7-0.91) Rate ratio vs. PBO: 0.79 (0.66-0.94); p=0.01	1.01 (0.89-1.15)
Secondary:		
-Time to first exacerbation-days (95% CI) -Estimated risk of exacerbation to wk. 104-% risk (95% CI) -HR for first exacerbation to wk. 104 (95%CI)	419 (332-530) 64.5% (57.5-71.4) 0.77 (0.64-0.93) P=0.009	321 68.3% (61.4-74.9)
↓ ≥ 2 pts in CAT Score-% response (95% CI)	41% OR response vs. PBO: 0.81 (0.6-1.09) NS	46%
↓ ≥ 4 pts in SGRQ Score- % response	50% No statistical analysis done *(refer to comments)* OR vs. PBO 1.17 (0.87-1.57)	46%
↓ ≥ 2 pts in E-RS Score-% response	31% No statistical analysis done *(refer to comments)* OR vs. PBO 0.82 (0.6-1.12)	34%
Annualized rate of exacerbations resulting in ED visit, hospitalization or both - events/yr (95% CI)	0.13 (0.10-0.18) No statistical analysis done *(refer to comments)* Rate ratio vs. PBO 0.65 (0.43-0.96)	0.2 (0.15-0.27)
Exploratory Analysis:		

Annualized rate of severe exacerbations-events/yr (95% CI)	0.10 Rate ratio 0.66 (0.42-1.01)	0.15

CAT=COPD assessment test measures impact of COPD symptoms on pts overall health; E-RS=evaluating respiratory symptoms measures overall severity of respiratory symptoms; OR=odds ratio; SGRQ=St George Respiratory Questionnaire measures impact of COPD on overall health, daily life and overall well-being.
Minimally important clinical difference (MCID-change in score): CAT: ≥ 2; E-RS: ≥ 2; SGRQ: ≥ 4

Comments

- Since the study enrolled patients during COVID, the rate of the primary endpoint was lower during COVID vs. before the pandemic. Therefore, the study duration was extended to up to 104 weeks for patients who had not yet had their exit appointment and for those enrolled after the change in study duration.
- For eligibility, moderate exacerbations were defined as the use of systemic corticosteroids with or without antibiotics; severe exacerbations were defined as hospitalization lasting at least 24 hours. As an endpoint, moderate exacerbations were defined as the use of systemic glucocorticoids, antibiotics or both; severe exacerbations were defined as hospitalization for at least 24 hours or death.
- Baseline characteristics: Exacerbations: 87% had ≥ 1 moderate; 19-21% had ≥ 1 severe. Modified medical research council (mMRC) dyspnea score of ≥ 2: 75-77%. Chronic bronchitis symptoms: 68-69%
- Other adjunctive therapies (azithromycin or PDE4 inhibitors) were permitted if started before randomization.
- According to the hierarchical statistical testing plan, since there was no statistically significant improvement in CAT score between groups, statistical analyses were not done on changes in subsequent secondary outcomes including SGRQ, E-RS or annualized rate of exacerbations requiring ED visit, hospitalization or both. However, no numeric differences were observed for these endpoints suggesting no differences of mepolizumab vs. PBO for improvement in symptoms or overall quality of life for any of these measures (CAT, SGRQ and E-RS).
- Additionally, exploratory outcomes of annualized rate of severe exacerbations and improvements in FEV_1 were not different between groups (not confirmatory).

Trial **METREX and MATREO (reported in a single publication)[3]**

Design Two phase III R, DB, MC, PC

Population Adults with COPD, FEV_1/FVC <0.7 before and after albuterol; $FEV_1 \geq 20\%$ but not >80% predicted after albuterol; ≥ 2 moderate exacerbations or ≥ 1 severe over the prior 12 months; receiving triple inhaler therapy with ICS/LABA/LAMA for at least 3 months before screening. *Patients with asthma were excluded.*
In METREX, stratification was based upon eosinophil type: count ≥ 150 mm^3 at screening or ≥ 300 mm^3 in past 12 months (eosinophilic phenotype) or eosinophil count <150 mm^3 at screening with no evidence for ≥ 300 mm^3 in past 12 months (non-eosinophilic phenotype).
In METREO, only patients with COPD and eosinophilic phenotype were included.

Intervention METREX: MEPO 100 mg q4w METREO: MEPO 100 or 300 mg q4w for 52 weeks

Comparator PBO q4w in both trials

Results

METREX	**Eosinophilic Phenotype (MOD ITT)**		**All Patients (MOD ITT)**	
Outcome Measure	Mepo 100 mg (n=233)	PBO (n=229)	Mepo 100 mg (n=417)	PBO (n=419)
Primary: Annualized rate moderate or severe exacerbation – events/yr	1.4 Rate ratio vs. PBO: 0.82 (0.68-0.98 P=0.04	1.71	1.49 Rate ratio vs. PBO: 0.98 (0.85-1.12) p>0.99	1.52
Secondary				
-Median time to first exacerbation – days -Estimated risk of exacerbation week 52 – percentage vs. PBO	192 64.6% (58.3-70.8) HR vs. PBO: 0.75 (0.6-0.94); p=0.04	141 75.2% (69.3-80.8)	194 65.5% (60.7-70.1) HR vs. PBO: 0.89 (0.75-1.05); p>0.99	176 71.2% (66.6-75.6)
Exacerbation leading to ED visit or hospital – events/yr (mean annual rate)	0.3 Rate ratio vs. PBO: 1.16 (0.77-1.75); p=0.6	0.26	0.29 Rate ratio vs. PBO: 1.10 (0.81-1.49); p>0.99	0.26
SGRQ Score 52 weeks Change from baseline	-2.8 p=>0.99	-3	-3.2 p>0.99	-4
CAT Score 52 weeks Change from baseline	-0.8 p=>0.99	0	-1 p>0.99	-0.4

METREO	**Eosinophilic Phenotype (MOD ITT)**		
Outcome Measure	Mepo 100 mg (n=223)	Mepo 300 mg (n=225)	PBO (n=226)
Primary: Annualized rate moderate or severe exacerbation – events/yr	1.19 Rate ratio vs. PBO: 0.8 (0.65-0.98) p=0.07 (NS)	1.27 Rate ratio vs. PBO: 0.86 (0.7-1.05) p=0.14 (NS)	1.49
Secondary *(See comments)*			
-Time to first exacerbation – days -Estimated risk of exacerbation week 52 – percentage vs. PBO	267 57.9% (51.5-64.5) HR 0.82 (0.64-1.04) p=0.14 (NS)	258 58.8% (52.4-65.3) HR 0.77 (0.6-0.97) p=0.14 (NS)	166 66.7% (60.2-73.1)
Exacerbation leading to ED visit or hospital – events/yr (mean annual rate)	0.17 Rate ratio vs. PBO: 0.59 (0.35-0.98) p=0.14 (NS)	0.23 Rate ratio vs. PBO: 0.83 (0.51-1.34) p=0.45 (NS)	0.28
SGRQ Score 52 weeks Change from baseline	-5 p=0.45 vs PBO (NS)	-3.3 p=0.93 vs PBO (NS)	-3.1
CAT Score 52 weeks Change from baseline	-1.6 p=0.93 vs PBO (NS)	-0.8 p=0.93 vs PBO (NS)	-0.4

	Comments	• In METREX, analyses were done separately for eosinophilic phenotypes and the overall study population with both eosinophilic and non-eosinophilic phenotypes included. • In METREX, there was no statistically significant improvement in exacerbation leading to ED visits or hospitalization between groups in either analysis (eosinophilic vs. overall population). Additionally, no statistical differences were observed in patient reported outcomes including improvement in SGRQ or CAT scores. • In METREO, there were no statistically significant differences between either dose of Mepo vs. PBO in the primary endpoint. Therefore, none of the results for the secondary endpoints were significant according to the prespecified multiple-testing plan.

SAFETY CONSIDERATIONS		
	Boxed Warnings	N/A
	Contraindications	History of hypersensitivity to mepolizumab or excipients in the formulation
	Other Warnings	Not indicated for treating acute symptoms or exacerbations of asthma or COPD. Risk for hypersensitivity reactions and opportunistic infections (e.g., herpes zoster). Pre-existing parasitic infection (Helminth) should be treated prior to initiating mepolizumab.
	Top 5 AEs	COPD Trials: back pain, diarrhea, cough, oropharyngeal pain and urinary tract infection
	Drug Interactions	No formal drug interaction studies have been done. However, population pharmacokinetic studies of Phase 3 trials did now show evidence of interaction of mepolizumab with small molecule medications.
	Clinical Trials	**MATINEE**: ADEs were reported in 74% Mepo and 77% PBO; most common ADE was exacerbation or worsening of COPD 12% and 15%, respectively; severe acute respiratory syndrome COVID infection (12% in each group); no anaphylaxis was reported; serious ADEs and pneumonia did not differ between groups; death occurred in 3% in each group. **MATREX and MATREO:** ADEs were reported in 80-83% in MATREX and 82-87% in MATREO. No differences in serious ADEs or deaths were reported. Most common ADEs were worsening of COPD, nasopharyngitis, headache and pneumonia.

PLACE IN THERAPY	DRUG	VANF	CFU	FDA Indications	GUIDELINES (COPD)
	Mepolizumab	NF	Not yet	Asthma, COPD, CRSwNP, EGPA, HES	Not yet included in COPD guidelines
	Dupilumab	NF	Y	Asthma, Atopic Dermatitis, Bullous Pemphigoid, COPD, CRSwNP, CSU, Eosinophilic Esophagitis, Prurigo Nodularis	GOLD COPD guideline 2025.[4] Patients with COPD exacerbations while receiving maximal inhaled therapies (LAMA+LABA+ICS), blood eosinophils ≥300 cells/microL and with chronic bronchitis.

CRSwNP=chronic rhinosinusitis with nasal polyps, CSU=chronic spontaneous urticaria, EGPA=eosinophilic granulomatosis with polyangiitis, HES=hypereosinophilic syndrome

VHA PLACE IN THERAPY		
	Potential Use in VHA	1. Patients with COPD with an eosinophilic phenotype (EOS ≥ 300 microL) who are continuing to have exacerbations despite adherence to maximal inhaled therapies (LAMA+LABA+ICS) with documented proper inhaler use technique. A trial of azithromycin and/or roflumilast should be considered prior to mepolizumab or dupilumab in certain patients with exacerbations of COPD *(Azithromycin may be used in patients with bronchiectasis or recurrent bacterial infections and a prior history of smoking; Roflumilast in patients with FEV_1 <50% and chronic bronchitis).*

References:

1. Mepolizumab NUCALA Prescribing Information. GlaxoSmithKline, LLC. Revised: May 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125526s007lbl.pdf Accessed September 3, 2025.
2. Sciurba FC, Criner GJ, Christenson FJ, et al. Mepolizumab to Prevention Exacerbations of COPD with an Eosinophilic Phenotype. N Engl J Med 2025;392:1710-1720.
3. Pavord ID, Chanez P, Criner GJ, et al. Mepolizumab for Eosinophilic Chronic Obstructive Pulmonary Disease. N Engl J Med 2017;377:1613-1629.
4. Global Initiative for Chronic Obstructive Lung Disease 2025. https://goldcopd.org/2025-gold-report/ Accessed September 3, 2025.

5. Dupilumab DUPIXENT Prescribing Information. Regeneron Pharmaceuticals, Inc. and Sanofi-Aventis, LLC. Revised: June 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761055s070lbl.pdf Accessed September 3, 2025.

Prepared: October 2025
Contact person: Catherine Kelley, PharmD, National PBM Clinical Pharmacy Program Manager, Formulary Management, VA Pharmacy Benefits Management Services (12PBM)