

FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Pulmonary-Allergy Drugs Advisory Committee (PADAC) Meeting

FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503)
10903 New Hampshire Avenue, Silver Spring, Maryland
July 25, 2018

QUESTIONS

1. **DISCUSSION:** Discuss the eosinophilic COPD phenotype (i.e., the relevance of peripheral blood eosinophils in COPD patients) and the criteria used in the mepolizumab program to define the patient population.

2. **DISCUSSION:** Discuss the efficacy of mepolizumab as add-on treatment to inhaled corticosteroid-based maintenance treatment for the reduction of exacerbations in patients with COPD guided by blood eosinophil counts. Include the following topics in your discussion:
 - a. the adequacy of dose exploration in COPD patients
 - b. the potential effect of unmeasured variables (e.g., lack of information regarding asthma history and oral corticosteroid use)
 - c. the lack of statistically significant results for the primary endpoint in one of the two trials
 - d. the clinical significance of the efficacy results (i.e., efficacy driven by moderate exacerbations)
 - e. lack of robust results for key secondary endpoints
 - f. efficacy results in the low eosinophil stratum that showed a numerical increase in COPD exacerbations
 - g. interpretation of the efficacy results given the uncertainty in the definition of the eosinophilic COPD phenotype

3. **VOTE:** Do the data provide substantial evidence of efficacy for mepolizumab as add-on treatment to inhaled corticosteroid-based maintenance treatment for the reduction of exacerbations in patients with chronic obstructive pulmonary disease (COPD) guided by blood eosinophil counts?
 - If no, what data are needed?

4. **VOTE:** Are the safety data adequate to support approval of mepolizumab as add-on treatment to inhaled corticosteroid-based maintenance treatment for the reduction of exacerbations in patients with chronic obstructive pulmonary disease (COPD) guided by blood eosinophil counts?
 - If no, what data are needed?

5. **VOTE:** Is the benefit-risk profile adequate to support approval of mepolizumab as add-on treatment to inhaled corticosteroid-based maintenance treatment for the reduction of exacerbations in patients with chronic obstructive pulmonary disease (COPD) guided by blood eosinophil counts?
 - If no, what data are needed?