



Issued: 09 December 2024 London UK

US FDA accepts GSK's submission for the use of *Nucala* (mepolizumab) in COPD

- Submission supported by MATINEE data showing significant and clinically meaningful reduction in annualised rate of moderate/severe exacerbations compared with placebo
 - *Nucala* could be the first approved biologic with monthly dosing for patients with COPD
 - COPD affects more than 14 million people in the US with estimates of 500,000 hospitalisations and up to 1.3 million emergency department visits each year
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GSK plc (LSE/NYSE: GSK) today announced the US Food and Drug Administration (FDA) has accepted for review, data from the MATINEE study to support the regulatory review process to obtain a new indication for the use of *Nucala* (mepolizumab), as an add-on maintenance treatment for patients with chronic obstructive pulmonary disease (COPD) with an eosinophilic phenotype. The Prescription Drug User Fee Act (PDUFA) date is 7 May 2025.

The submission is based on data from the MATINEE study, which evaluated the efficacy and safety of mepolizumab in 804 patients with COPD who have evidence of type 2 inflammation characterised by blood eosinophil count.¹ The trial recruited COPD patients with broad clinical presentations including hard to treat patients with emphysema-only, chronic bronchitis only, or a mix of both. The MATINEE study met its primary endpoint with the addition of mepolizumab to inhaled maintenance therapy, achieving a statistically significant and clinically meaningful reduction in the annualised rate of moderate/severe exacerbations versus placebo with patients treated for 52-104 weeks.

IL-5 is a key cytokine (protein) in type 2 inflammation, an inflammatory process exhibited in up to 40% of patients with COPD and the underlying pathobiology that drives symptoms and exacerbations.²⁻⁴ Type 2 inflammation is typically detected by blood eosinophil count, a biomarker, which can be measured by a simple blood test. This test can help indicate a COPD patient's risk of exacerbation and deterioration, their response to treatment, and inform treatment strategies in these patients.⁵

COPD affects more than 390 million people globally and over 14 million people in the US, exerting a significant burden on healthcare resources and the lives of patients.⁶⁻⁹ Recurrent exacerbations add to pressures on healthcare systems and account for a large proportion of the annual direct medical costs of COPD with emergency department visits and inpatient care costing the US healthcare system around \$7 billion a year.^{6,8,9}

The full results of MATINEE will be presented at a future scientific congress and form the basis of regulatory submissions around the world.

Nucala is currently approved for use in the US across four IL-5 mediated conditions. These include two respiratory indications as an add-on maintenance treatment for patients with severe asthma with an eosinophilic phenotype aged 6 years and older and as an add-on maintenance treatment for adult patients with chronic rhinosinusitis with nasal polyps (CRSwNP) and inadequate response to nasal corticosteroids. Indications also include the use of *Nucala* for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA) and for the treatment of patients ages 12 years and older with hypereosinophilic syndrome (HES) for ≥ 6 months without an identifiable non-hematologic secondary cause.¹² *Nucala* is currently not indicated for COPD anywhere in the world.

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About chronic obstructive pulmonary disease (COPD) and type 2 inflammation

COPD is a progressive and heterogenous inflammatory lung disease that includes chronic bronchitis and emphysema, and is the third leading cause of death resulting in more than 3 million deaths annually.^{5,7} Patients with COPD experience persistent respiratory symptoms such as breathlessness, cough, and sputum along with progressive airflow obstruction due to the chronic inflammation that impact daily life.⁵ Exacerbations are acute episodes of worsening COPD symptoms and can result in hospitalisation and irreversible lung damage that leads to progressive lung function decline. Exacerbations can result in a cycle of deterioration in overall physical health and increased mortality.^{5,12} Many patients experience persistent symptoms and exacerbations meaning there is a need for targeted therapies to address the underlying pathophysiology linked to disease progression.^{5,13-15}

Type 2 inflammation is present in a variety of immuno-inflammatory conditions and is the underlying pathology that drives symptoms and exacerbations in up to 40% of people with COPD.² Blood eosinophil count is a biomarker for type 2 inflammation that can be easily measured by a simple blood test for levels of a type of white blood cell called eosinophils. IL-5 is a core cytokine (protein) in type 2 inflammation alongside IL-4 and IL-13.² IL-5 is responsible for the growth, activity, and survival of eosinophils and there is now evidence to show IL-5 has broad effects on other immune and structural cell types beyond eosinophils, including those that contribute to inflammation, lung remodelling and disease progression.^{2,15-20} The individual role of these cell types has not been definitively established in COPD.

About *Nucala*

First approved in 2015 for severe asthma with an eosinophilic phenotype in the US, mepolizumab is a monoclonal antibody that targets and binds to interleukin-5 (IL-5), a key messenger protein (cytokine) in type 2 inflammation. *Nucala* has been developed for the treatment of a range of IL-5 mediated diseases associated with type 2 inflammation.

About the mepolizumab development programme for COPD

The mepolizumab program in COPD is comprised of three clinical trials. The first two studies, METREX and METREO, completed in 2017. MATINEE was designed to supplement METREX and METREO, building on our learnings from these studies and IL-5 science to identify the patients who could benefit the most from *Nucala* and support future submissions and approvals for use in this indication.²¹

For product and important safety information please consult the country relevant summary of product characteristics.

US information available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/125526s004lbl.pdf

About GSK in respiratory

GSK continues to build on decades of pioneering work to deliver more ambitious treatment goals, develop the next generation standard of care, and redefine the future of respiratory medicine for hundreds of millions of people with respiratory diseases. With an industry-leading respiratory portfolio and pipeline of vaccines, targeted biologics and inhaled medicines, we are focused on improving outcomes and the lives of people living with all types of asthma and COPD along with less understood refractory chronic cough or rarer conditions like systemic sclerosis with interstitial lung disease. GSK is harnessing the latest science and technology with the aim to modify underlying disease dysfunction and prevent disease progression.

About GSK

GSK is a global biopharma company with a purpose to unite science, technology, and talent to get ahead of disease together. Find out more at gsk.com.

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Cautionary statement regarding forward-looking statements

GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Such factors include, but are not limited to, those described under Item 3.D "Risk factors" in GSK's Annual Report on Form 20-F for 2023, and GSK's Q3 Results for 2024.

Registered in England & Wales:

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