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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 annualized 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 hospitalizations and up to 1.3 million emergency department visits each year

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 characterized 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 annualized 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.

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 hospitalization 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.

NUCALA is indicated in the U.S. for the:

- add-on maintenance treatment of adult and pediatric patients aged 6 years and older with severe asthma and with an eosinophilic phenotype. NUCALA is not indicated for the relief of acute bronchospasm or status asthmaticus.
- add-on maintenance treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients 18 years of age and older with inadequate response to nasal corticosteroids.
- treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).
- treatment of adult and pediatric patients aged 12 years and older with hypereosinophilic syndrome (HES) for ≥6 months without an identifiable non-hematologic secondary cause.

Important Safety Information

The following information is based on the US Prescribing Information for Nucala in licensed indications only. Please consult the full Prescribing Information for all the labelled safety information for Nucala.

CONTRAINDICATIONS
Known hypersensitivity to mepolizumab or excipients.

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions
Hypersensitivity reactions (eg, anaphylaxis, angioedema, bronchospasm, hypotension, urticaria, rash) have occurred with NUCALA. These reactions generally occur within hours of administration but can have a delayed onset (ie, days). Discontinue if a hypersensitivity reaction occurs.

Acute Asthma Symptoms or Deteriorating Disease
NUCALA should not be used to treat acute asthma symptoms, acute exacerbations, or acute bronchospasm.

Opportunistic Infections: Herpes Zoster
Herpes zoster infections have occurred in patients receiving NUCALA. Consider vaccination if medically appropriate.

Reduction of Corticosteroid Dosage
Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of therapy with NUCALA. Decreases in corticosteroid doses, if appropriate, should be gradual and under the direct supervision of a physician. Reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.

Parasitic (Helminth) Infection
Treat patients with pre-existing helminth infections before initiating therapy with NUCALA. If patients become infected while receiving NUCALA and do not respond to anti-helminth treatment, discontinue NUCALA until infection resolves.

ADVERSE REACTIONS

Most common adverse reactions (≥5%) in patients receiving NUCALA:

- Severe asthma trials: headache, injection site reaction, back pain, fatigue
- CRSwNP trial: oropharyngeal pain, arthralgia
- EGPA and HES trials (300 mg of NUCALA): no additional adverse reactions were identified to those reported in severe asthma clinical trials

Systemic reactions, including hypersensitivity, occurred in clinical trials in patients receiving NUCALA. Manifestations included rash, pruritus, headache, myalgia, flushing, urticaria, erythema, fatigue, hypertension, warm sensation in trunk and neck, cold extremities, dyspnea, stridor, angioedema, and multifocal skin reaction. A majority of systemic reactions were experienced the day of dosing.

USE IN SPECIFIC POPULATIONS
The data on pregnancy exposures are insufficient to inform on drug-associated risk. Monoclonal antibodies, such as mepolizumab, are transported across the placenta in a linear fashion as the pregnancy progresses; therefore, potential effects on a fetus are likely to be greater during the second and third trimesters.

Please see the full Prescribing Information **and** Patient Information **for NUCALA for more information, or ask your healthcare provider.**

About the mepolizumab development program 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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