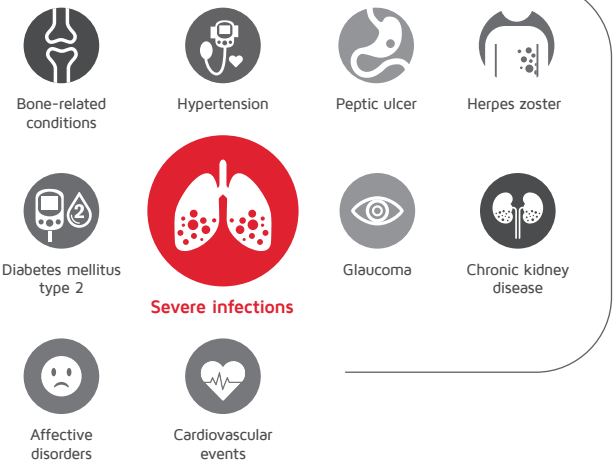
Significant morbidity in severe asthma with low dose OCS exposure

The ORs of all outcomes* associated with current OCS use, except cataract, were also increased in patients who had only received an average of 1 prescription per year, a cumulative dose < 500 mg, and/or an average daily dose ≤1 mg within 2 years before the index date.[1]

Even 1 prescription of OCS per year could lead to an increased risk of severe infection[1]**

2X***

Support the need of developing new treatments for severe asthma with a better safety profile than that of OCS.[1]



OCS, oral corticosteroid; OR, odd ratio

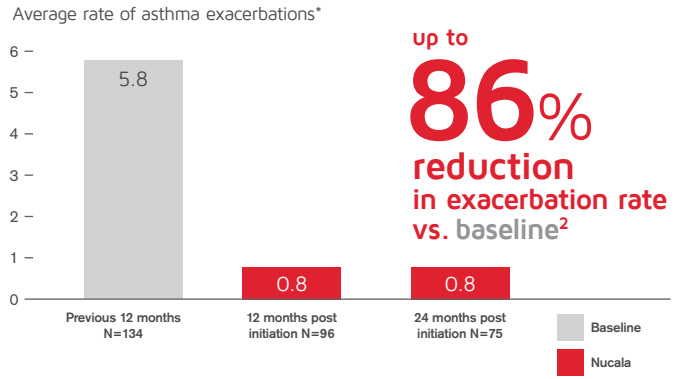
*Outcomes of interest include bone-related conditions, hypertension, peptic ulcer, severe infections, herpes zoster, diabetes mellitus type 2, cataract, glaucoma, chronic kidney disease, affective disorders, cardiovascular events.

**Main analysis: incident Read code of an infection preceded or followed within 1 month by a record suggesting hospitalisation or i.v. anti-infective treatment. Sensitivity analysis restricted to patients with IHS linkage (conducted in the nested-case control study only): incident Read code of an infection preceded or followed within 1 month by a hospitalisation whose reason was infection (ICD-10 code of infection in the IHS data).

***After adjusting for confounding, current oral prednisolone use was most strongly associated with an increased risk of severe infection, compared with non-use of prednisolone; OR 2.16 (95% CI, 2.05–2.27).

Choose Nucala to reduce exacerbation rate

Real-World Evidence: France ATU (2 years)[2]

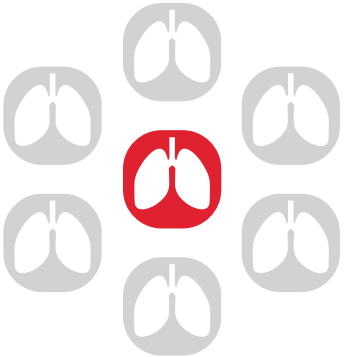


up to 86% reduction in exacerbation rate vs. baseline[2]

ATU, Temporary Authorisation for Use; OCS, oral corticosteroid; ED, emergency department.

*Defined as those requiring ED visit/hospitalisation and/or use of OCS for ≥48 hours or an increase of ≥50% in daily OCS dose. Average exacerbations/patient/year: 5.8 ± 4.4 at baseline (over the previous 12 months) vs 0.8 ± 1.1 (over the first 12 months after the first injection) and 0.8 ± 0.9 between 12 and 24 months.

Reduction from 7 to 1 exacerbations per year



- Reduce OCS bursts
- Reduce hospitalization / ED visits
- Reduce the increase of ≥50% in daily OCS dose

Nucala
mepolizumab

Fixed dose & monthly injection for your patients

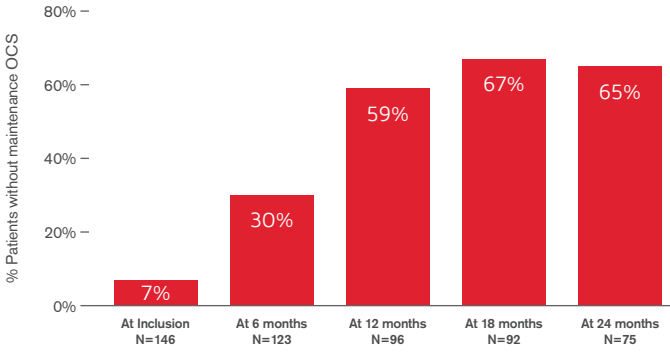
Available in pre-filled pen: Easy-to-use & At-home administration

Choose Nucala to free patients from OCS

Real-World Evidence: France ATU (2 years)[2]

Reduce and even eliminate OCS use[2]

Proportion of patients without maintenance OCS in France ATU study



up to **65%** of patients **free** from **OCS** at 2 years vs baseline[2]

n=75 n=49/75 (65.3%) at 24 months

Mean daily dose of OCS:
20.6 ± 16.5 mg at inclusion
8.3 ± 15.9 mg at 12 months
7.8 ± 17.0 mg at 24 months

5 out of 8 patients free from OCS

ATU, Temporary Authorisation for Use; OCS, oral corticosteroid.

Safety Information for Nucala® (Mepolizumab)

▪ Nucala should not be used to treat acute asthma exacerbations ▪ Asthma-related adverse events or exacerbations may occur during treatment. Patients should be instructed to seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment ▪ Abrupt discontinuation of corticosteroids after initiation of Nucala therapy is not recommended ▪ Eosinophils may be involved in the immunological response to some helminth infections and patients with pre-existing helminth infections should be treated before starting therapy ▪ The most commonly reported adverse reactions during treatment were headache, injection site reactions and back pain ▪ Local injection site reactions occurred mainly at the start of treatment and within the first 3 injections with fewer reports on subsequent injections.

Abbreviated prescribing information

NAME OF THE PRODUCT Nucala **QUALITATIVE AND QUANTITIVATIVE COMPOSITION** Each 1ml of pre-filled pen contains 100mg of mepolizumab. **INDICATIONS** Nucala is indicated as an add-on treatment for severe refractory eosinophilic asthma in adults and adolescents aged 12 years and older. **POSOLOGY AND METHOD OF ADMINISTRATION** *Adults* The recommended dose of mepolizumab is 100mg administered subcutaneously every 4 weeks. Nucala is intended for long-term treatment. The need for continued therapy should be considered at least on an annual basis as determined by physician assessment of the patient's disease severity and level of control of exacerbations. *Paediatric population* The safety and efficacy of Nucala in children less than 12 years old have not been established. *Elderly patients (>65 years)* No dose adjustment. *Renal and hepatic impairment* No dose adjustment. Nucala pre-filled pen should be used for subcutaneous injection only. Nucala may be self-administered by the patient or administered by a caregiver if their healthcare professional determines that it is appropriate, and the patient or caregiver are trained in injection techniques. For self-administration the recommended injection sites are the abdomen or thigh. A caregiver can also inject Nucala into the upper arm. **CONTRAINDICATIONS** Hypersensitivity to the active substances or to any of the excipients. **WARNINGS AND PRECAUTIONS** Nucala should not be used to treat acute asthma exacerbations. Asthma-related adverse events or exacerbations may occur during treatment. Patients should be instructed to seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment. Abrupt discontinuation of corticosteroids after initiation of Nucala therapy is not recommended. Reduction in corticosteroid doses, if required, should be gradual and performed under the supervision of physician. Hypersensitivity and administration-related reactions Acute and delayed systemic reactions, including hypersensitivity reactions (e.g. anaphylaxis, urticaria, angiodema, rash, bronchospasm, hypotension) have occurred following administration of Nucala. These reactions generally occur within hours of administration, but in some instances have a delayed onset (i.e., typically within several days). These reactions may occur for the first time after a long duration of treatment. Parasitic infections Eosinophils may be involved in the immunological response to some helminth infections. Patients with pre-existing helminth infections should be treated before starting therapy. If patients become infected whilst receiving treatment with Nucala and do not respond to anti-helminth treatment, temporary discontinuation of therapy should be considered. **INTERACTIONS** No interaction studies have been performed. Cytochrome P450 enzymes, efflux pumps and protein-binding mechanisms are not involved in the clearance of mepolizumab. Increased levels of pro-inflammatory cytokines (e.g. IL-6), via interaction with their cognate receptors on hepatocytes, have been shown to suppress the formation of CYP450 enzymes and drug transporters, however, elevation of systemic pro-inflammatory markers in severe asthma is minimal and there is no evidence of IL-5 receptor alpha expression on hepatocytes. The potential for drug-drug interactions with mepolizumab is therefore considered low. **FERTILITY, PREGNANCY AND LACTATION** Pregnancy There is a limited amount of data (less than 300 pregnancy outcomes) from the use of mepolizumab in pregnant women. Mepolizumab crosses the placental barrier in monkeys. Animal studies do not indicate reproductive toxicity. The potential for harm to a human fetus is unknown. As a precautionary measure, it is preferable to avoid the use of Nucala during pregnancy. Administration of Nucala to pregnant women should only be considered if the expected benefit to the mother is greater than any possible risk to the fetus. Breast-feeding There are no data regarding the excretion of mepolizumab in human milk. However, mepolizumab was excreted into the milk of cynomolgous monkeys at concentrations of less than 0.5% of those detected in plasma. A decision must be made whether to discontinue breast-feeding or to discontinue Nucala therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. Fertility There are no fertility data in humans. Animal studies showed no adverse effects of anti-IL5 treatment on fertility. **ADVERSE REACTIONS** The frequency of adverse reactions is defined using the following convention: very common (≥1/10), common (≥1/100 to <1/10) and uncommon (≥1/1000 to <1/100). Infections & infestations: Common: Lower respiratory tract infection, urinary tract infection, pharyngitis Immune system disorders: Common: Hypersensitivity reactions (systemic allergic)* Nervous system disorders: Very common: Headache Respiratory, thoracic and mediastinal disorders: Common: Nasal congestion Gastrointestinal disorders: Common: Abdominal pain upper Skin and subcutaneous tissue disorder: Common: Eczema Musculoskeletal and connective tissue disorders: Common: Back pain General disorders and administration site conditions: Common: Administration-related reactions (systemic non allergic)**, local injection site reactions, pyrexia. **OVERDOSE** There is no clinical experience with overdose of mepolizumab. Single doses of up to 1500 mg were administered intravenously in a clinical trial to patients with eosinophilic disease without evidence of dose-related toxicities. There is no specific treatment for an overdose with mepolizumab. If overdose occurs, the patient should be treated supportively with appropriate monitoring as necessary. Further management should be as clinically indicated or as recommended by the national poisons centre, where available. * Systemic reactions including hypersensitivity have been reported at an overall incidence comparable to that of placebo. ** The most common manifestations associated with reports of systemic non-allergic administration-related reactions were rash, flushing and myalgia; these manifestations were reported infrequently and in <1% of subjects receiving mepolizumab 100 mg subcutaneously. Abbreviated Prescribing Information based on Nucala Prescribing Information (HK072017(GDS12/EMA20191118)).

Reference: 1. Bloechliger et al. Respiratory Research 2018; 19:75 **2.** Taille C et al. Eur Respir J 2020; 55:1902345.

Nucala
mepolizumab

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