Report NUCALA® mepolizumab

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: mepolizumab **Brand Name:** Nucala **Originator/licensee:** GlaxoSmithKline Trading Services **Classification:** NI **ATC code:** R03DX09 **Orphan Status:** **Eu:** No **Us:** No **Mechanism of action:** mepolizumab prevents IL-5 from binding to the alpha chain of the IL-5 receptor complex expressed on the eosinophil cell surface and thus inhibits IL-5 signaling and the overexpression of peripheral blood and tissue eosinophils. Neutralizing IL-5 reduces the promotion, growthand survival of eosinophils in blood, sputum and other tissues, although complete blood eosinopenia isnot possible due to redundant signaling by IL-3 and GM-CSF through a common β-sub-unit [1].	**Authorized Indication:** **EMA:** mepolizumab is indicated as an add-on therapy with intranasal corticosteroids for the treatment of adult pts with severe CRSwNP for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control [2]. **FDA:** mepolizumab is indicated for the add-on maintenance treatment of adult patients 18 years and older with CRSwNP[3]. **Route of administration:** SC **Licensing status** **EU CHMP P.O. date:** 16/09/2021 **FDA M.A. date:** 29/07/2021 **EU Speed Approval Pathway: - FDA Speed Approval Pathway: -** **ABBREVIATIONS:** **AEs:** Adverse Events **CHMP:** Committee for Medicinal Products for Human Use **CI**: Confidence Interval **COPD:** Chronic Obstructive Pulmonary Disease **CRS**: Chronic Rhinosinusitis **CRSwNP:** Chronic Rhinosinusitis with nasal polyps **GM-CSF:**Granulocyte-Macrophage Colony-Stimulating Factor **HES**: Hypereosinophilic syndrome **IL-3:** Interleukin-3 **IL-5**: Interleukin-5 **ITT:** Intention-To-Treat **M.A.:** Marketing Authorization **P.O.:** Positive Opinion **Pts:** patients **SAEs**: Serious Adverse Events **SoC**: Standard of Care **VAS**: Visual Analog Scale **vs**: versus	**Summary of clinical EFFICACY:** **SYNAPSE (NCT03085797)** was a randomized, double blind, placebo-controlled, parallel group, phase III trial. Eligible pts (≥18 years; *n*=414) had recurrent, refractory, severe bilateral nasal polyp symptoms (nasal obstruction symptom VAS* score of >5), were eligible for repeat nasal surgery (overall symptoms VAS score >7 and endoscopic nasal polyps score of ≥5, with a minimum score of two in each nasal cavity), despite SoC treatment, and had to have at least one nasal surgery in the past 10 years. Pts were randomly assigned (1:1) to receive either 100 mg mepolizumab subcutaneously (*n*=206) or placebo (*n*=201) once every four weeks, in addition to SoC (mometasone furoate intranasal spray for at least eight weeks before screening and during the study, saline nasal irrigations, systemic corticosteroids or antibiotics, or both) for 52 weeks. The coprimary endpoints were change from baseline in total endoscopic nasal polyp score at week 52 and in mean nasal obstruction VAS score during weeks 49-52, assessed in the ITT population. Total endoscopic nasal polyp-score significantly improved at week 52 from baseline with mepolizumab vs. placebo (adjusted difference in median scores based on quantile regression -0.73; 95% CI -1.11 to -0.34; *p*<0.0001) and nasal obstruction VAS score during weeks 49-52 also significantly improved (-3.14;95% CI -4.09 to -2.18; *p*<0.0001) [4]. **The VAS is a validated, subjective measure for acute and chronic pain. Scores are recorded by making a handwritten mark on a 10-cm line that represents a continuum between "no pain" and "worst pain.* **Summary of clinical SAFETY:** The proportion of pts who had on-treatment AEs was similar between the two groups [169 (82%) in the mepolizumab group and 168 (84%) in the placebo group]. The most frequently reported AEs in the two arms were nasopharyngitis (25% in the mepolizumab arm vs. 23% in the placebo arm), headache (18% vs. 22%, respectively), epistaxis (8% vs. 9%, respectively), sinusitis (5% vs. 11%, respectively). AEs considered related to study treatment by the investigator were reported in 30 (15%) pts receiving mepolizumab and 19 (9%) receiving placebo. On-treatment SAEs occurred in 12 (6%) pts receiving mepolizumab and 13 (6%) receiving placebo; none were considered related to mepolizumab. One death was reported in the placebo group (myocardial infarction), however not considered related to the study treatment [4]. **Ongoing studies:** ● ***For the same indication:***Yes ● ***For other indications:***Yes **Discontinued studies (for the same indication):**No **References:** 1. https://www.ema.europa.eu/en/documents/assessment-report/nucala-epar-public-assessment-report_en.pdf 2. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/nucala-0 3. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761122s006,125526s018lbl.pdf 4. https://www.thelancet.com/article/S2213-2600(21)00097-7/fulltext 5. https://gallery.farmadati.it/Home.aspx 6. Peters A. T.Diagnosis and management of rhinosinusitis: a practice parameter update. Annals of Allergy, Asthma & Immunology, 2014-10-01 7. https://www.io.nihr.ac.uk/wp-content/uploads/2020/06/4298-Mepolizumab-for-Nasal-Polyposis-V1.0-MAY2020-NON-CONFdocx.pdf 8. https://clinicaltrials.gov/ct2/home	**Cost of therapy:** In Italy, the price for one vial of mepolizumab 100 mg (subcutaneous powder for injection) is 1,792.47 €, corresponding to the price of one-month therapy [5]. **Epidemiology:** CRSwNP is a subtype of CRS affecting approximately 2-4% of the general population [4]. ----- **POSSIBLE PLACE IN THERAPY** Medical treatment options for pts with CRSwNP remain limited. The initial treatment with either topical steroids(e.g. mometasone furoate nose drops or spray) or nasal saline irrigation is recommended in order to reduce symptoms and signs, improve quality of life and prevent disease progression or recurrence. If the nose drops or spray are ineffective, oral therapy with corticosteroids for up to two weeks should be considered [6,7]. **OTHER INDICATIONS IN DEVELOPMENT:** Yes(Asthma, HES, COPD, Eosinophilic Granulomatosis with Polyangiitis) [8]. **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:-** **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** Yes (CBP-201, Tezepelumab, Omalizumab, Etokimab, Benralizumab) [8]. *Service reorganization Y/N: Yes *Possible off label use Y/N: Yes

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