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 **OrphanStatus:** **Eu:** No **Us:** No **Mechanism of action:** mepolizumabprevents 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:** mepolizumabis indicated as an add-on treatment for adult pts with inadequately controlled HES without an identifiable non-haematologic secondary cause[2]. **FDA:** mepolizumabis indicated for the treatment of adult and pediatric patients aged ≥12 year with HES for ≥6 months without an identifiable non-hematologic secondary cause[3]. **Route of administration:**IV **Licensing status** **EU CHMP P.O. date:** 16/09/2021 **FDA M.A. date:** 25/09/2020 **EU Speed Approval Pathway:** - **FDA Speed Approval Pathway: -** ----- **ABBREVIATIONS:** **AE:** Adverse events **CHMP:** Committee for Medicinal Products for Human Use **COPD:** Chronic obstructive pulmonary disease **FIP1L1-PDGFRA:**FIP1-like-1-platelet-derived growth factor receptor a fusion gene **GM-CSF:**Granulocyte-Macrophage Colony-Stimulating Factor **HES:** Hypereosinophilic syndrome **IL-3:** Interleukin-3 **IL-5**: Interleukin-5 **M.A.:** Marketing Authorization **P.O.:** Positive Opinion **pts:** patients **SC:** subcutaneous **SoC:** standard of care therapy **vs.:** versus	**Summary of clinical EFFICACY:** **NCT02836496** is a randomized, multicenter, double-blind, placebo-controlled, phase 3 trial, in adolescent and adult pts with HES receiving SoC.Eligible pts had FIP1L1-PDGFRA-negative HES, experienced two or more flares(worsening of HES-related symptomsorblood eosinophil count requiring therapeutic escalation) in the previous 12 months, and had a screening blood eosinophil count ≥1000 cells/mL. Pts were randomized to SC mepolizumab(300 mg; n=54) or placebo(n=54) every 4 weeks for 32 weeks, plus existing HES-therapy.The primaryoutcomewas the proportion of pts with one or more flaresduring the study, inaddition, pts who withdrew early from the study were countedas having a flare. The proportion of pts experiencing ≥1 flares/withdrawing from the study was 50% lower with mepolizumab[15 of 54 (28%)] vs. placebo [30 of 54 (56%); p=0.002] [4]. **Summary of clinical SAFETY:** AEs were similar between groups (89% in mepolizumabarm vs.87% in placebo arm). Serious AEs occurred in 19% pts in mepolizumabarm vs. 15% in placebo arm, none were considered drug-related. The most frequently reported non-serious AEswere (mepolizumab arm vs. placebo arm): bronchitis(8% vs. 10%), upper respiratory tract infection (8% vs. 2%), headache (7% in both arm), nasopharyngitis (7% in both arm), pain in extremity (6% vs. 2%), diarrhea(5% vs. 7%), and rhinitis(5% vs. 6%)[4]. **Ongoing studies:** ● ***For the same indication:***Yes ● ***For other indications:***Yes [Phase III, but if it is an O/OE drug, also Phase II] **Discontinued studies (for the same indication):**- --- **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/2020/761122s005lbl.pdf 4. Roufosse, Florence et al. "Efficacy and safety of mepolizumab in hypereosinophilic syndrome: A phase III, randomized, placebo-controlled trial." The Journal of allergy and clinical immunology vol. 146,6 (2020): 1397-1405. doi:10.1016/j.jaci.2020.08.037 5. https://gallery.farmadati.it/Home.aspx 6. https://www.orpha.net/orphacom/cahiers/docs/IT/Prevalenza_delle_malattie_rare_in_ordine_alfabetico.pdf 7. https://www.io.nihr.ac.uk/wp-content/uploads/2020/02/20556-TSID_9918-Mepolizumab-for-Severe-Hypereosinophilic-Syndrome-V1.0-JAN2020-NON-CONF.pdf 8. https://clinicaltrials.gov/ct2/results?cond=&term=&type=Intr&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&age_v=&gndr=&intr=Mepolizumab&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=2&rsub=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort= 9. https://clinicaltrials.gov/ct2/results?cond=HES+-+Hypereosinophilic+Syndrome&term=&type=Intr&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&age_v=&gndr=&intr=&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=1&phase=2&rsub=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort=	**Cost of therapy:** In Italy, mepolizumabis available in different pharmaceutical forms: • 100mg/ml solution for injection pre-filled pen - €1,792.47 • 100mg/1ml solution for injection pre-filled syringes - €1,792.47 • 100mg powder for solution for injection vials - €1,792.47 *All retail prices include VAT*[5]. The recommended dose of mepolizumabis 300 mg administered once every 4 weeks by SC injection as three separate 100 mg injections [3], so onemonth therapy costs5,377.41€ for any pharmaceutical form chosen. **Epidemiology:** At January 2021, in Europe the prevalence of HES was 1.5/100,000 [6] ----- **POSSIBLE PLACE IN THERAPY** The treatment and management of HES varies based on the severity of the condition and ifan underlying cause for the eosinophilia has been identified. Prednisolone, indicated for the treatment and/or suppression ofinflammatory and allergic disorders, is utilized to treat HES. Imatinib is indicated for the treatment of adult pts withadvanced HES and/or chronic eosinophilic leukaemia with FIP1L1-PDGFRA (P/F)rearrangement [7]. **OTHER INDICATIONS IN DEVELOPMENT:**COPD, Asthma, Churg-Strauss Syndrome [8] **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:**- **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION :** Benralizumab, Ruxolitinib [9] *Service reorganization Y/N No *Possible off label use Y/N Yes, in pts aged ≥ 12 years.

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