Report XROMI® - Hydroxycarbamide

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: Hydroxycarbamide **Brand Name:** Xromi **Originator/licensee:** Nova Laboratories Ireland Limited **Classification:** NI **ATC code:** L01XX05 **Orphan Status:** **Eu:** No **Us:** No **Mechanism of action:** Hydroxycarbamide blocks the growth and reproduction of some cells, such as blood cells. Although the way that it works in this disease is not fully understood, hydroxycarbamide can reduce the numbers of cells that are circulating in the blood, as well as prevent red blood cells changing shape in pts with sickle cell disease. This reduces the risk of blood vessels becoming blocked. [1]	**Authorized Indication:** **EMA:** Hydroxycarbamide is indicated for the prevention of vaso-occlusive complications of Sickle Cell Disease in patients aged >9 months. [2] **FDA: -** **Route of administration:** OS **Licensing status** **EU CHMP P.O. date:**22/02/2024 **FDA M.A. date:** - **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** - --- **ABBREVIATIONS:** **AE:** adverse event **CHMP:** Committee for Medicinal Products for Human Use **CTCAE:** Common Terminology Criteria for Adverse Events **HbF:** fetal hemoglobin **M.A.:** Marketing Authorization **MTD:** Maximum Tolerated Dose **P.O.:** Positive Opinion **Pts:** patients **SCA:** Sickle Cell Anaemia **SCD:** Sickle Cell Disease **SD:** standard deviation	**Summary of clinical EFFICACY:** **NCT03763656:**is a phase II, multi-center, open-label, prospective study where children between 6 months to 18 years with sickle cell anemia (HbSS or HbS/β0), previously hydroxyurea naïve, were eligible for recruitment. Exclusion criteria included renal or hepatic insufficiency. A total of 32 pts were recruited; all participants were black (African American, Caribbean or Black British). At study enrollment, the overall mean (SD) baseline HbF was 11.9% (8.7). MTD with target myelosuppression was achieved by 20 (62.5%) study participants overall. All study participants started liquid hydroxyurea at 15 mg/kg once daily, with dose escalation every 8-12 weeks until MTD was achieved (absolute neutrophil count 1-3 × 109 /L or a maximum dose of 35 mg/kg/day). Treatment continued for 12 - 15 months. The primary outcome measures were pharmacokinetic parameters. A total of 464 plasma hydroxyurea concentrations were available for pharmacokinetic modelling. The model predicted hydroxyurea $AUC_{(0\text{-}inf)}$ increased with age (and body weight), although the distribution of exposures overlapped considerably across age categories. Age did not significantly influence C_{max}. The dose normalized AUC at steady state estimated in this study was 4.3 µg.h/ml/mg, comparable to previously reported values of 4.6 and 4.9 µg.h/ml/mg. [3] **Summary of clinical SAFETY:**all except one of the 32 study participants experienced at least one AE, the most common being vaso-occlusive crisis. There were 28 related AEs in nine participants, the most frequent of which were isolated and transient occurrences of hematological toxicity, with no serious infections and resulted in temporary dose interruption, dose reduction or no change in dose. Cytopenias were typically associated with recent and concurrent respiratory or viral illness. All serious AEs (seven in total) and most of the CTCAE Grade ≥3 AEs were unrelated to hydroxyurea and indicative of the typical complications of SCA. Indeed, the results of this study support a dose escalation approach. Dose escalation to MTD is more efficacious than fixed dosing, without increasing the risk of infections or toxicities and is routinely recommended in treatment algorithms. [3] **Ongoing studies:** ● ***For the same indication:*** Yes ● ***For other indications:*** No **Discontinued studies (for the same indication):** No --- **References:** [1] https://www.ema.europa.eu/en/documents/overview/xromi-epar-medicine-overview_en.pdf [2] https://www.ema.europa.eu/en/documents/smop/chmp-post-authorisation-summary-positive-opinion-xromi-ii-19_en.pdf [3] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10424132/pdf/main.pdf [4] https://gallery.farmadati.it/Home.aspx [5] https://www.osservatoriomalattierare.it/malattie-rare/anemia-falciforme	**Cost of therapy:**20 cps of hydroxycarbamide 500mg cost € 5,74 (ex-factory price)[4]. **Epidemiology:**The number of SCD sufferers in Italy ranges between 2,500 and 4,000 people [5]. In the Veneto region, the number of pts is estimated between 200 and 320 per year. **POSSIBLE PLACE IN THERAPY:**Hydroxycarbamide is a first-line treatment to prevent vaso-occlusive complications of Sickle Cell Disease in pts aged ≥2 years. Xromi could be considered a first-line treatment for this indication in children aged >9 months. **OTHER INDICATIONS IN DEVELOPMENT: -** **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT**: - **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** - *Service reorganization: No *Possible off label use: Yes