POST-AUTHORISATION SAFETY STUDY (PASS)

Annual Progress Report

STUDY OVERVIEW

Title	Non-interventional Post-Authorisation Safety Study of Burosumab in the Treatment of Children with X-linked Hypophosphataemia (XLH)
Version of the progress report	Version 1.0
Date of last version of the progress report	Not applicable
European Union electronic Register of Post-Authorisation Studies (EU PAS)/ European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) register number	To be confirmed
Active substance	Active substance: burosumab - recombinant human IgG1 monoclonal antibody to fibroblast growth factor 23 ATC code: M05BX05: Drug for the treatment for bone diseases, other drugs affecting bone structure and mineralization
Medicinal product	Invented name: Crysvita Pharmaceutical form and strength: 10, 20 and 30 mg/mL solution for injection in vials

This study was conducted in accordance with all relevant regulatory requirements, including, where applicable, the Declaration of Helsinki (and its amendments), the guideline on good pharmacovigilance practices (GVP) Module VIII – post-authorisation safety studies, and the guidelines for good pharmacoepidemiology practice (GPP) (ISPE).

Product reference	Not Available
Procedure number	EMEA/H/C/004275
Joint PASS	No
Research question and objectives	**Primary objectives:** 1. To evaluate the frequency and severity of safety outcomes in paediatric patients with XLH and radiographic evidence of bone disease who are aged 1 year of age and older and adolescents with growing skeletons, treated with burosumab, including but not limited to: death, hospitalizations, cardiovascular disease, cancer [all sites], hyperphosphataemia and its complications, ectopic mineralization and increased parathyroid hormone levels 2. To prospectively evaluate the frequency and outcomes of pregnancies in female patients treated with burosumab 3. To prospectively evaluate the frequency and severity of safety outcomes in patients with mild to moderate chronic kidney disease at baseline treated with burosumab **Secondary objective:** To perform a retrospective cohort study using data from the registry to compare the safety outcomes of interest in patients exposed to burosumab to those in patients receiving alternative treatments for XLH
Country(-ies) of study	Belgium, Denmark, Finland, France, Germany, Italy, Netherlands, Norway, Spain, Sweden and United Kingdom (UK)
Author	IQVIA on behalf of the Marketing Authorisation Holder

MARKETING AUTHORISATION HOLDER(S)

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PASS PROGRESS INFORMATION

Protocol version and date	Version 1.0; 15-August-2018 (Sub-study to the parent XLH Registry Protocol-Version 3.0; 15-February-2019)
Approval date/s (approved by Committee for Medicinal Products for Human Use [CHMP])	13-December-2018
Data cut-off date	18-August-2019
No. of patients enrolled	15 (8 in France; 7 in United Kingdom)
No. of exposed patients/ the no. of patients presenting the outcome	8 received burosumab
Recruitment	Active, recruiting
Adverse event (AE)	No AEs recorded
Protocol deviation/s	No protocol deviation recorded
Problems/ Bottlenecks encountered	**Triggers for PASS eligibility:** • Registry amended protocol approved, protocol v3.0 dated 15-February-2019 • Sites to receive adequate training on protocol v3.0 for the Registry and the PASS • Patients to sign the last informed consent form (ICF) (re-consent for already enrolled patients) last ICFs v3.0 04-February-2019 for Parents and Adults and v2.0 10-January-2019 for minors • Burosumab to be available at country level. Not all countries have burosumab available – burosumab launch dates to be followed accurately and any Early Access Program to be known

	• Only children and adolescents are now in the PASS, not the adult population **Bottlenecks:** • Burosumab is not available in all enrolling countries in the Registry • For the patients enrolled in a country where Burosumab is available (UK, France, Italy, Sweden); reconsenting would be required to be part of the PASS • The re-consenting takes time. Even if remote re-consenting is proposed, sites wanted to have a face to face visit with their patients to re-consent them. This may need some months to have re-consenting in place. • Some physicians are not interested to be part of the PASS
Planned interim/ final Analysis report	• First interim report of study results to be submitted after 50 patients under burosumab have achieved at least 6 months of time in the PASS. Trigger not met – no interim analysis performed – hence no interim report. Interim report expected in 2020. • Second interim report of study results to be submitted after 5 years, i.e. December 2023 • December 2028
Results of any planned interim analysis of study data before or after the end of data collection	No reports; No analysis