# Progress Report

Xarelto Paediatric VTE PASS Drug Utilization Study: An observational, longitudinal, multi-source drug utilization safety study to evaluate the drug use patterns and safety of rivaroxaban oral suspension in children under two years with venous thromboembolism (XAPAEDUS).

## 1. Objectives

The primary objectives in this study are to describe:

- Clinical characteristics and demographics of patients using anticoagulation therapy for the treatment of venous thromboembolism –VTE– (rivaroxaban oral suspension or standard of care (SOC))
- Use of anticoagulation therapy (including selected drug, dose, and duration) for treatment of VTE
- Incidence and severity of bleeding (major bleeding, and clinically relevant non-major bleeding) according to anticoagulation therapy (rivaroxaban oral suspension or SOC)

The secondary objectives in this study are to describe:

- Time trends in patient characteristics and anticoagulation treatment patterns at the population-level over the study period
- Incidence of recurrent symptomatic VTE according to anticoagulation therapy (rivaroxaban oral suspension or SOC)
- Specialty and care setting of physicians who prescribe anticoagulation therapy (rivaroxaban oral suspension or SOC)

## 2. Data sources

The study will use secondary data derived from France, Sweden, Denmark, and Spain:

- **Denmark** – National Patient Register (NPR). The Danish NPR has full coverage of the population of Denmark, 5.8 million, since 1977. It has data available on hospital admissions and discharges, emergency and outpatient visits, inpatient treatments, and procedures. It also allows linkage for prescription drugs at community pharmacy level, drugs administered in outpatient setting and deaths.
- **Sweden** – National Patient Register. The Swedish NPR has full coverage of the population of Sweden, 10.3 million people, since 1987. It includes inpatient and specialized outpatient care, information on admissions, discharges, and medical procedures. It can also be linked to other data sources to obtain information on all prescribed drugs dispensed at pharmacies, and information on deaths.
- **France** – Système National Des Données De Santé (SNDS). SNDS has full coverage of the population of France, 67 million, since 2006. It holds information on treatment in outpatient and inpatient setting (although inpatient only available for costly innovative drugs), medical procedures, and medical summaries of all hospitalizations from public and private hospitals. Information on deaths is also available through external linkage.
- **Catalonia (Spain)** – Sistema d'Informació per al Desenvolupament de la Investigació en Atenció Primària (SIDIAP). SIDIAP covers 75% of the population of Catalonia (Spain),

approximately 5.8 million, since 2006. It contains anonymized healthcare data collected by healthcare physicians from 328 primary care Centers in Catalonia. It holds information on diagnoses, prescriptions, and diagnostic procedures, but can also be linked with hospital discharge data and hospital medication for outpatient dispensation.

## 3. Project Milestones

The core protocol of the project was approved on the 16th of November 2022. Below table presents planned milestones for the project.

| Milestone | Planned date/ Actual date |
|---|---|
| Start of study period | Market entry date of rivaroxaban oral suspension in each country:<br>• Denmark: October 2021<br>• Sweden: September 2021<br>• France: April 2022<br>• Spain: June 2022 |
| Start of data collection | Q4 2023* |
| End of data collection | Q2 2029 |
| Study progress report 1 | Q4 2023 |
| Study progress report 2 | Q4 2024 |
| Study progress report 3 | Q4 2025 |
| Study progress report 4 | Q4 2026 |
| Study progress report 5 | Q4 2027 |
| Final report of study results | Estimated Q4 2029 |

(*) Time needed for data access process (applications, approvals) and other tasks to launch the study.

## 4. Progress by country

The data access process is planned to be completed by end of Q4 2023 for all data sources except for SNDS which is planned for end of Q1 2024 due to a longer contracting process.

The actual study size for the study will depend on the number of patients that meet inclusion criteria in each country. Actual patient counts are not yet available for all data sources as the study is still in the set-up phase.

## 5. Challenges encountered and deviations:

One of the key objectives of the annual progress reports will be to identify opportunities to finalize the study earlier. In parallel with the follow-up of the overall uptake of rivaroxaban oral suspension, the number of children under two years with VTE and those among them receiving rivaroxaban oral suspension will be monitored annually as far as possible and reported in annual progress reports.

In Spain, rivaroxaban oral suspension is not reimbursed, so it is only available since June 2022 on the private market. This lack of reimbursement could have an impact on the final number of patients, potentially resulting in fewer patients than initially anticipated in SIDIAP, which was an average total of 45 children under two years with VTE (lowest and highest estimate range: 17-73), with 15 of them receiving rivaroxaban oral suspension (range 6-25), and 1 of them with a bleeding with hospitalization (range 0-1) throughout the whole study period (2023-2027). We will continue to monitor the uptake of rivaroxaban oral suspension in the private market in Spain.