Population Pharmacokinetics of Recombinant Fusion Protein Linking Coagulation Factor IX with Recombinant Albumin (rIX-FP) in Adult and Pediatric Patients with Severe Hemophilia B

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Objectives: rIX-FP was developed to extend the half-life of FIX, improving hemophilia B treatment by allowing less frequent dosing than the standard FIX products. Four trials in the PROLONG-9FP clinical program were completed in previously treated adult and pediatric patients with hemophilia B (FIX ≤ 2%). A population pharmacokinetics (PPK) model was developed to characterize rIX-FP pharmacokinetics (PK), to describe and identify demographic and clinical covariates of rIX-FP PK variability and to simulate FIX activity-time profiles for various dosing regimens.

Methods: Blood PK samples from 104 patients were collected to determine the plasma FIX activity using a validated one-stage clotting assay. PPK modeling was performed using NONMEM 7, including the assessment of potential covariates on rIX-FP PK. Visual predictive check (VPC) was used for model evaluation.

Results: A 2-compartmental model appropriately described the rIX-FP PK. Body weight was a significant covariate on clearance and both central and peripheral volumes of distribution, and weight-adjusted dose was a significant covariate on central volume. The VPC results confirmed model stability, and the PK parameters were estimated with good precision. For the respective age groups of ≥12 y, 6 to <12 y and <6 y, simulations based on the final PPK model predicted a median exogenous trough activity of 8, 4 and 2% after 75 IU/kg rIX-FP once every 14 days and 14, 8, and 5% after 40 IU/kg once weekly. Time to 1% after a single dose was also estimated.

Conclusions: The PPK model adequately characterized rIX-FP PK. This model can be utilized as a tool to simulate FIX activity-time profiles for various dosing scenarios of rIX-FP.

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