INTRODUCTION

Eslicarbazepine acetate (ESL) is a once-daily O-1,4-epideuteric antiepileptic drug (AED), approved as adjunctive treatment in adults ≥18 years for partial-onset seizures (POS) in the USA and Canada, and as monotherapy in the USA. In Europe, ESL is approved as adjunctive therapy in adults, adolescents, and children aged 3 years and above, with POS with or without secondary generalization.

The safety and efficacy of ESL as an adjunctive treatment has been studied in pediatric populations and is supported for subjects ≥12 years by population pharmacokinetic (PPK) modeling of the plasma concentration of eslicarbazepine, the primary ESL metabolite.

A modeling and simulation strategy with separate ESL/antidepressant (top-down) approach and physiologically based pharmacokinetics (PBPK) prediction (bottom-up approach) was employed, using data from pediatric patients and adults, in order to inform dose selection and design of a clinical trial (Study 002-036) in infant and pediatric patients aged 1 month–14 years with POS.

OBJECTIVES

To refine the previously developed pediatric PPK model to predict eslicarbazepine PK in infant patients.

To develop a PEM model for eslicarbazepine in healthy adults and pediatric patients.

To predict eslicarbazepine exposures using the pediatric PEM and PPK models, in order to inform ESL dose selection and the design of Study 363 assessing ESL as an adjunctive therapy in infants.

METHODS

Modeling and simulation strategy to inform dose and sample selection

An overview of the modeling and simulation strategy is shown in Figure 1, and the model development steps are outlined in Figure 2.

RESULTS

Proposed dosing regimen

The proposed dosing regimen for Study 363, based on modeling and simulations, for the low and high maintenance doses in each age group are shown in Table 1.

REFERENCES


