A Phase 1 Study to Evaluate Bioequivalence Between RHV-0223 40 mg Zydus® Sublingual Formulation and Riluzole 50 mg Oral Tablet in Healthy Volunteers

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Background

Zydus® (Rilutek®) is a racemic mixture of a single 40 mg sublingual dose of riluzole which is indicated for the treatment of amyotrophic lateral sclerosis (ALS). Zydus® is approved for treatment of ALS in the US and Canada, but not in Europe. Biohaven (RHV-0223) is a single 40 mg racemic mixture, designed to reduce food effect and PK variability compared to Zydus®. The objective of this study was to evaluate the bioequivalence of RHV-0223 40 mg sublingual vs oral tablets.

Methods

Objectives

Primary

Secondary and exploratory

Subjects

N=138

Study design and treatments

Part 1: RHV-0223 40 mg sublingual

Part 2: RHV-0223 40 mg sublingual and 10 mg sublingual

Part 3: RHV-0223 40 mg swallows tablets

Table 1. Subject demographics

Table 2. PK parameters for RHV-0223 and Rilutek

Conclusions

• The RHV-0223 40 mg sublingual rapidly dissolving zydus formulation of riluzole is bioequivalent to riluzole 50 mg oral tablets.

Table 3. Geometric LS mean ratios and 90% CI for AUC0–∞, AUC0–t, and Cmax

Table 4. Summary of adverse events

References

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Zydus® is a registered trademark of R.P. Scherer Technologies, Inc.

Figure 1. Study design

Figure 2. Subject disposition

Figure 3. Riluzole plasma concentrations over time for RHV-0223 and Rilutek under Fasted and Fed conditions

Figure 4. Riluzole plasma concentrations over time for RHV-0223 under Fed and Fed conditions

Figure 5. Safety

Figure 6. Summary of adverse events

Table 5. Commonly reported AEs

Figure 7. AEs by treatment area

Conclusions

Safety

• All 138 subjects who received ≥1 dose of study drug reported a total of 350 AEs.

• 17% of the total number of AEs were reported by 5 subjects (RHV-0223 n=4; Rilutek n=1).

• No clinically meaningful laboratory abnormalities after oral RHV-0223 swallowed tablets.

• All adverse events are thought to be pharmacologically related and were not associated with functional changes. Of the 151 related AEs, 125 were observed for RHV-0223 (Table 4).

• Of the 94 related AEs observed for Rilutek, 83 were observed for RHV-0223, and were not associated with functional changes. Of the 145 related AEs, 126 were observed for Rilutek (Table 4).

• No clinically significant medical history were excluded.

• Clinical chemistry, urinalysis, vital signs, physical examination, and electrocardiography were performed throughout the study.

• All adverse events were thought to be no clinically meaningful

• No clinically meaningful changes in laboratory values, vital signs, physical measurements, or electrocardiograms were observed.

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