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Draft Guidance on Ponesimod

October 2024

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Active Ingredient: Ponesimod

Dosage Form: Tablet

Route: Oral

Strengths: 2 mg, 3 mg, 4 mg, 5 mg, 6 mg 7 mg, 8 mg, 9 mg, 10 mg, 20 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 2 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Exclude subjects with abnormal complete blood count or liver function tests. Exclude subjects with electrocardiogram abnormalities (e.g., bradycardia [or heart rate <50 beat per minute] or atrioventricular conduction abnormalities). Monitor for four hours after dosing for signs and symptoms of bradycardia with hourly pulse and blood pressure measurements. Female subjects of reproductive potential should use non-hormonal contraception during the study and continue to use effective contraception for two weeks after the last dose. Subjects should be informed not to use live attenuated vaccines at least 1 month prior, during, and for up to 2 weeks after the study. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of ponesimod. Alternatively, a parallel study design may be considered.

Analyte to measure: Ponesimod in plasma

Bioequivalence based on (90% CI): Ponesimod

Waiver request of in vivo testing: 3 mg, 4 mg, 5 mg, 6 mg 7 mg, 8 mg, 9 mg, 10 mg and 20 mg strengths based on (i) acceptable bioequivalence study on the 2 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths

Dissolution test method and sampling times: The dissolution information for this drug product can be found in the FDA's Dissolution Methods database, http://www.accessdata.fda.gov/scripts/cder/dissolution/. Conduct comparative dissolution testing on 12 dosage units for each of all strengths of the test product and reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

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[1] If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions*.