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Draft Guidance on Fingolimod Lauryl Sulfate

October 2024

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Active Ingredient: Fingolimod lauryl sulfate

Dosage Form: Tablet, orally disintegrating

Route: Oral

Strengths: EQ 0.25 mg Base, EQ 0.5 mg Base

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: EQ 0.5 mg Base
   Subjects: Healthy males and healthy females not of reproductive potential
   Additional comments: The orally disintegrating tablet should be placed on the tongue, allowed to disintegrate, and swallowed without water. Exclude subjects with abnormal blood counts or liver function tests. Exclude subjects with electrocardiogram abnormalities. Monitor for six hours after dosing for signs and symptoms of bradycardia with hourly pulse and blood pressure measurements. Subjects should be informed not to use live attenuated vaccines during and for up to 2 months after the study. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of fingolimod. Alternatively, a parallel study design may be considered.

Analytes to measure: Fingolimod and its active metabolite, fingolimod-phosphate in whole blood by using an achiral assay

Submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}.

Bioequivalence based on (90% CI): Fingolimod

Waiver request of in vivo testing: EQ 0.25 mg Base strength based on (i) acceptable bioequivalence study on the EQ 0.5 mg Base strength, (ii) acceptable in vitro dissolution testing of both strengths, and (iii) proportional similarity of the formulations between both 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 both 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*.