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Draft Guidance on Fingolimod Lauryl Sulfate

November 2023

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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 Studies:	Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: EQ 0.5 mg Base
   Subjects: Healthy males and females not of reproductive potential
   Additional comments: The orally disintegrating tablet should be placed directly on the tongue, allowed to dissolve, 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.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: EQ 0.5 mg Base
Subjects: Healthy males and females not of reproductive potential
Additional comments: See comments above.

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 Cmax.

Bioequivalence based on (90% CI): Fingolimod

Waiver request of in vivo testing: EQ 0.25 mg Base strength based on (i) acceptable bioequivalence studies 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 two 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 each of both strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.

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