Contains Nonbinding Recommendations

Draft Guidance on Fingolimod

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

Active Ingredient: Fingolimod

Dosage Form; Route: Capsule; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 0.5 mg x 1 capsule (0.5 mg dose)
   Subjects: Healthy males, non-pregnant and non-lactating females, general population.
   Additional Comments: 1. Fingolimod has a long terminal elimination half-life ($t_{1/2}$). Please ensure adequate washout periods between treatments in the crossover studies. You may also consider using a parallel study design. 2. The study protocols and informed consent documents should include adequate information pertaining to the warnings and precautions as described in the approved drug label of this product.

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2. Type of study: Fed
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 0.5 mg x 1 capsule (0.5 mg dose)
   Subjects: Healthy males, non-pregnant and non-lactating females, general population.
   Additional Comments: Please see comment above.

Analytes to measure (in appropriate biological fluid): Fingolimod and its active metabolite, fingolimod-phosphate in whole blood

Please 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: Not Applicable

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods website available to the public at the following location: http://www.accessdata.fda.gov/scripts/cder/dissolution/. Conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).