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Draft Guidance on Simvastatin

October 2024

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Active Ingredient: Simvastatin

Dosage Form: Tablet, orally disintegrating

Route: Oral

Strengths: 10 mg, 20 mg, 40 mg, 80 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: 80 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: The orally disintegrating tablet should be placed on the tongue, allowed to disintegrate, and swallowed with water. Females of reproductive potential should use effective contraception during the study.

Analytes to measure: Simvastatin and its metabolite, beta-hydroxyacid in plasma

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): Simvastatin

Waiver request of in vivo testing: 10 mg, 20 mg, and 40 mg strengths based on (i) acceptable bioequivalence study on the 80 mg strength, (ii) acceptable dissolution testing across all strengths, and (iii) proportional similarity in 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) products.[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.*