

Guidance on Simvastatin

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Active ingredient: Simvastatin

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover *in-vivo*
Strength: 80 mg
Subjects: Normal healthy males and females, general population
Additional Comments:

2. Type of study: Fed
Design: Single-dose, two-way crossover *in-vivo*
Strength: 80 mg
Subjects: Normal healthy males and females, general population
Additional comments:

Analytes to measure : Simvastatin and its beta-hydroxyacid metabolite in plasma. Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the beta-hydroxy metabolite of simvastatin, 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: 5 mg, 10 mg, 20 mg, 40 mg based on (i) acceptable bioequivalence studies on the 80 mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

Dissolution test method and sampling times:

Please conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products using the method specified in the USP method.