

Contains Nonbinding Recommendations
Draft – Not for Implementation
Draft Guidance on Ezetimibe; Simvastatin
October 2024

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Active Ingredients:	Ezetimibe; Simvastatin
Dosage Form:	Tablet
Route:	Oral
Strengths:	10 mg; 10 mg, 10 mg; 20 mg, 10 mg; 40 mg, 10 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: 10 mg; 80 mg
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: Females of reproductive potential should use effective contraception during the study.

Analytes to measure: Ezetimibe (unconjugated), total ezetimibe (ezetimibe + ezetimibe glucuronide), simvastatin, and simvastatin acid (β -hydroxy acid) in plasma

Bioequivalence based on (90% CI): Ezetimibe (unconjugated), total ezetimibe (ezetimibe + ezetimibe glucuronide), and simvastatin

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