

Contains Nonbinding Recommendations

Draft Guidance on Atorvastatin Calcium

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Atorvastatin Calcium

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in-vivo
Strength: EQ 80 mg Base
Subjects: Healthy males and nonpregnant females, general population
Additional Comments: Applicants may consider using a reference-scaled average bioequivalence approach for this drug product. If using this approach, please provide evidence of high variability in the bioequivalence parameters of AUC and/or C_{max} (i.e., within-subject variability $\geq 30\%$). For general information on this approach, please refer to the Individual Product Bioequivalence Recommendations Guidance on Progesterone Capsules.

2. Type of study: Fed
Design: Single-dose, two-way crossover in-vivo
Strength: EQ 80 mg Base
Subjects: Healthy males and nonpregnant females, general population.
Additional Comments: Please see additional comments above.

Analytes to measure (in appropriate biological fluid): Atorvastatin and its active metabolites, ortho and para- hydroxylated atorvastatin in plasma

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 C_{max}.

Bioequivalence based on (90% CI): Atorvastatin

Waiver request of in-vivo testing: EQ 10 mg, 20 mg and 40 mg Base based on (i) acceptable bioequivalence studies on the EQ 80 mg Base 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:

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Please find the dissolution information for this product at this website. Please 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 application.