

Contains Nonbinding Recommendations
Draft – Not for Implementation
Draft Guidance on Atorvastatin Calcium
October 2024

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Active Ingredient:	Atorvastatin calcium
Dosage Form:	Tablet
Route:	Oral
Strengths:	EQ 10 mg Base, EQ 20 mg Base, EQ 40 mg Base, EQ 80 mg Base
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: EQ 80 mg Base
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: Applicants may consider using a reference-scaled average bioequivalence approach. If using this approach, provide evidence of high variability in the pharmacokinetic parameters (i.e., within-subject variability $\geq 30\%$) for the reference listed drug. For detailed information on this approach, refer to the most recent version of the FDA guidance for industry on *Bioequivalence Studies with Pharmacokinetic Endpoints for Drugs Submitted Under an ANDA*.^a

Analytes to measure: Atorvastatin and its active metabolites, ortho and para- hydroxylated atorvastatin 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): Atorvastatin

Waiver request of in vivo testing: EQ 10 mg Base, EQ 20 mg Base and EQ 40 mg Base strengths, based on (i) acceptable bioequivalence study 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: 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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^a For the most recent version of a guidance, check the FDA guidance website at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>.

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*.