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Draft Guidance on Darunavir

October 2024

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Active Ingredient: Darunavir

Dosage Form: Tablet

Route: Oral

Strengths: 75 mg, 150 mg, 300 mg, 400 mg, 600 mg, 800 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 800 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Single doses of both the test product and reference listed drug (RLD) should be administered with ritonavir 100 mg twice daily. The ritonavir dosing should be started at least two days before administration of darunavir tablet and maintained until the end of pharmacokinetic sampling of each treatment. 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 ≥30%) for the RLD. 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]

Analyte to measure: Darunavir in plasma

Bioequivalence based on (90% CI): Darunavir

Waiver request of in vivo testing: Darunavir tablet, 75 mg, 150 mg, 300 mg, 400 mg, and 600 mg, based on (i) acceptable bioequivalence study on the 800 mg strength, (ii) acceptable in vitro dissolution testing across 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 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*.