Draft Guidance on Cobicistat; Darunavir; Emtricitabine; Tenofovir Alafenamide Fumarate

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This guidance, which interprets the Agency's regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

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This is a new draft product-specific guidance for industry on generic cobicistat; darunavir; emtricitabine; tenofovir alafenamide fumarate.

Active Ingredients:	Cobicistat; Darunavir; Emtricitabine; Tenofovir alafenamide fumarate
Dosage Form; Route:	Tablet; oral
Recommended Studies:	Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 150 mg; 800 mg; 200 mg; EQ 10 mg Base
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Exclude subjects with any combination of abnormal liver function tests, a history of drug-induced skin reactions or allergic reactions to sulfa drugs. Applicants may consider using a reference-scaled average bioequivalence approach for darunavir. If using this approach, provide evidence of high variability in the pharmacokinetic parameters (i.e., within-subject variability ≥30%) for the reference

product. 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]

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 150 mg; 800 mg; 200 mg; EQ 10 mg Base
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: See comments above.

Analytes to measure: Cobicistat, darunavir, emtricitabine, and tenofovir alafenamide in plasma

Bioequivalence based on (90% CI): Cobicistat, darunavir, emtricitabine, and tenofovir alafenamide

Waiver request of in vivo testing: Not applicable

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 the test and reference products. Specifications will be determined upon review of the ANDA.

Unique Agency Identifier: PSG_210455

[a] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.