Contains Nonbinding Recommendations

Draft Guidance on Efavirenz; Lamivudine; Tenofovir Disoproxil Fumarate

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

Active Ingredients: Efavirenz; Lamivudine; Tenofovir disoproxil fumarate

Dosage Form; Route: Tablet; oral

Recommended Study: One study

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 400 mg; 300 mg; 300 mg
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: Ensure adequate washout periods between treatments in the crossover studies due to efavirenz's long terminal elimination half-life. For either a crossover or parallel study, sample collection time should be adequate to ensure completion of gastrointestinal transit of the drug product and absorption of the drug substance. Collect sufficient blood samples in the bioequivalence studies to adequately characterize the peak concentration (C_{max}) and time to reach peak concentration (t_{max}).

Analytes to measure (in appropriate biological fluid): Efavirenz, lamivudine, and tenofovir in plasma

Bioequivalence based on (90% CI): Efavirenz, lamivudine, and tenofovir

Waiver request of in vivo testing: Not applicable

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods website, available to the public at the following location: 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 abbreviated new drug application.