

Draft Guidance on Aliskiren Hemifumarate; Hydrochlorothiazide

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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: Aliskiren Hemifumarate; Hydrochlorothiazide

Form/Route: Tablets/Oral

Recommended studies: 3 studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover *in-vivo*
Strength: 300 mg/25 mg
Subjects: Healthy males and nonpregnant females, general population.
Additional Comment:

2. Type of study: Fed
Design: Single-dose, two-way crossover *in-vivo*
Strength: 300 mg/25 mg
Subjects: Healthy males and nonpregnant females, general population.
Additional Comments: The test and reference products should be administered 30 minutes after start of the meal.

3. Type of study: Fasting
Design: Single-dose, two-way crossover *in-vivo*
Strength: 300 mg/12.5 mg
Subjects: Healthy males and nonpregnant females, general population.
Additional Comment

Analytes to measure: Aliskiren and hydrochlorothiazide in plasma

Bioequivalence based on (90% CI): Aliskiren and hydrochlorothiazide

Waiver request of in-vivo testing: 150 mg /25 mg; and 150 mg/12.5 mg based on (i) acceptable bioequivalence studies on the 300 mg/25 mg strength, (ii) acceptable dissolution testing across all strengths, and (iii) proportional similarity in 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.