

Draft Guidance on Amlodipine Besylate, Hydrochlorothiazide, Olmesartan Medoxomil

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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: Amlodipine Besylate, Hydrochlorothiazide, Olmesartan Medoxomil

Form/Route: Tablet/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in-vivo
Strength: 10 mg (base), 25 mg, 40 mg
Subjects: Healthy males and nonpregnant females, general population.
Additional Comments: Females should practice abstention or contraception during the study.

2. Type of study: Fed
Design: Single-dose, two-way crossover in-vivo
Strength: 10 mg (base), 25 mg, 40 mg
Subjects: Healthy males and nonpregnant females, general population.
Additional Comments: Please see comment above.

Analytes to measure (in appropriate biological fluid): Amlodipine, Hydrochlorothiazide and Olmesartan in plasma

Bioequivalence based on (90% CI): Amlodipine, Hydrochlorothiazide and Olmesartan

Waiver request of in-vivo testing:

Amlodipine Besylate, Hydrochlorothiazide, Olmesartan Medoxomil 10 mg (base), 12.5 mg, 40 mg; 5 mg (base), 25 mg, 40 mg; 5 mg (base), 12.5 mg, 40 mg; 5 mg (base), 12.5 mg, 20 mg based on (i) acceptable bioequivalence studies on the Amlodipine Besylate, Hydrochlorothiazide, Olmesartan Medoxomil 10 mg (base), 25 mg, 40 mg strength tablet, (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:

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.

Note:

Due to safety concerns the subjects should remain in a comfortable recumbent position for up to 8 hours after dosing and remain under medical surveillance for up to 12 hours after dosing. Before they are allowed to ambulate, they should sit up with legs in a dependent position for one minute prior to standing up. While standing immobile, they should be closely observed for blood pressure changes and/or orthostatic symptoms, including nausea, dizziness, or faintness for at least three minutes.