

Draft Guidance on Hydrochlorothiazide, Irbesartan

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Tablet/Oral

Recommended studies: 2 studies

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

2. Type of study: Fed
Design: Single-dose, two-way crossover in-vivo
Strength: 12.5 mg/300 mg
Subjects: Healthy males and nonpregnant females, general population.
Additional Comments: Please refer to the Amantadine Hydrochloride Tablet Draft Guidance for additional information regarding fed studies.

Analytes to measure (in appropriate biological fluid): Hydrochlorothiazide and irbesartan in plasma

Bioequivalence based on (90% CI): Hydrochlorothiazide and irbesartan

Waiver request of in-vivo testing: 12.5 mg/150 mg based on (i) acceptable bioequivalence studies on the 12.5 mg/300 mg strength, (ii) acceptable in-vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths. Please refer to the Mirtazapine Tablet Draft Guidance for additional information regarding waivers of in vivo testing.

Please note that per Docket No. FDA-2011-P-0822, the FDA determined that the 25 mg/300 mg strength of AVALIDE was not withdrawn from sale for safety or effectiveness reasons. Should a sponsor choose to pursue approval of this strength, the above studies can be performed using the RLD 12.5/150 mg x 2 vs. the test 25 mg/300 mg. The 12.5 mg/300 mg and 12.5 mg/150 mg are then eligible for a waiver of in-vivo testing as outlined above.

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.