

Guidance on Drospirenone; Estradiol

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Active ingredient: Drospirenone; Estradiol

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover *in-vivo*
Strength: 0.5 mg; 1 mg
Subjects: Normal healthy postmenopausal women
Additional Comments:

2. Type of study: Fed
Design: Single-dose, two-way crossover *in-vivo*
Strength: 0.5 mg; 1 mg
Subjects: Normal healthy postmenopausal women
Additional Comments:

Analytes to measure (in appropriate biological fluid): Drospirenone and unconjugated estradiol, unconjugated estrone and total estrone in plasma.

Bioequivalence based on (90% CI): Drospirenone and baseline-adjusted total estrone.

Statistical analysis should be performed on data both with and without baseline adjustment. Bioequivalence acceptance criteria will be based on baseline-adjusted results only.

Baseline adjustment: Data of each subject and period should be adjusted for the mean of -1 hour, -0.5 hour and predose levels for that same subject and period. If, after adjustment, any negative concentrations result, they should be set equal to zero.

Waiver request of in-vivo testing: Not Applicable

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at <http://www.fda.gov/cder/ogd/index.htm>. 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.