

Contains Nonbinding Recommendations

Draft Guidance on Estradiol

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in-vivo
Strength: 2 mg
Subjects: Healthy, physiologically or surgically postmenopausal females
Additional Comments:

2. Type of study: Fed
Design: Single-dose, two-way crossover in-vivo
Strength: 2 mg
Subjects: Healthy, physiologically or surgically postmenopausal females
Additional Comments:

Bioequivalence based on (90% CI): Baseline-adjusted Estrone (total)

Please submit the estradiol (unconjugated) and estrone (unconjugated) data as supportive evidence of comparable therapeutic outcome. For the estradiol (unconjugated) and estrone (unconjugated), the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and Cmax.

Waiver request of in-vivo testing: 0.5 mg and 1 mg based on (i) acceptable bioequivalence studies on the 2 mg strength, (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.