

Draft Guidance on Ethinyl Estradiol; Norethindrone

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in-vivo
Strength: 0.035 mg/1 mg (28 tablet packet)
Subjects: Normal healthy postmenopausal women
Additional Comments:

2. Type of study: Fed
Design: Single-dose, two-way crossover in-vivo
Strength: 0.035 mg/1 mg (28 tablet packet)
Subjects: Normal healthy postmenopausal women.
Additional Comments:

Analytes to measure (in appropriate biological fluid): Ethinyl Estradiol and Norethindrone in plasma.

Bioequivalence based on (90% CI): Ethinyl Estradiol and Norethindrone

Waiver request of in-vivo testing: 0.035 mg/0.5 mg and 0.035 mg/0.75 mg, and .035 mg/1 mg based on (i) acceptable bioequivalence studies on the 0.035 mg/1 mg strength, (ii) acceptable dissolution testing across all strengths, and (iii) proportional similarity in the formulations across all strengths.

Please note that Ethinyl Estradiol and Norethindrone Tablets, 0.035 mg/1 mg and 0.035 mg/0.5 mg, 0.035 mg/0.75 mg, and 0.035 mg/1 mg are the subject of two separate reference products. Two separate applications must be submitted comparing to the appropriate reference products. An applicant may request a waiver of in vivo bioequivalence testing for generic of these RLDs provided that it (1) submits an ANDA containing acceptable in vivo studies on the 0.035 mg/1 mg strength; (2) cross-references the ANDA for the 0.035 mg/1 mg strength; and (3) meets the criteria of 21 CFR § 320.22(d)(2). Please refer to the Guidance for Industry, *Variations in Drug Products that May Be Included in a Single ANDA* located at:

Contains Nonbinding Recommendations

Draft Guidance on Ethinyl Estradiol; Norethindrone

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072892.pdf>

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.