

*Contains Nonbinding Recommendations*

**Draft Guidance on Ethinyl Estradiol; Levonorgestrel**

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

**Form/Route:** Tablets/Oral

**Recommended studies:** 4 studies

1. Type of study: Fasting  
Design: Randomized, single-dose, two-way crossover, *in-vivo*  
Strength: 0.03 mg; 0.125 mg EE/LNG  
Subjects: Normal healthy non-pregnant females, general population.  
Additional Comments:

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2. Type of study: Fasting  
Design: Randomized, single-dose, two-way crossover, *in-vivo*  
Strength: 0.04 mg; 0.075 mg EE/LNG  
Subjects: Normal healthy non-pregnant females, general population.  
Additional Comments:

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3. Type of study: Fed  
Design: Randomized, single-dose, two-way crossover, *in-vivo*  
Strength: 0.03 mg; 0.125 mg EE/LNG  
Subjects: Normal healthy non-pregnant females, general population.  
Additional Comments:

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4. Type of study: Fed  
Design: Randomized, single-dose, two-way crossover, *in-vivo*  
Strength: 0.04 mg; 0.075 mg EE/LNG  
Subjects: Normal healthy non-pregnant females, general population.  
Additional Comments:

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**Analytes to measure:** Levonorgestrel and ethinyl estradiol in plasma.

**Bioequivalence based on (90% CI):** Levonorgestrel and ethinyl estradiol

**Waiver request of in-vivo testing:** 0.03 mg/0.05 mg based on (i) acceptable bioequivalence studies on the 0.03 mg/0.125 mg and 0.04 mg/0.075 mg strengths, (ii) proportional similarity in the formulations of all strengths, and (iii) acceptable *in vitro* dissolution testing of 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.