Draft Guidance on Ethinyl Estradiol; Levonorgestrel

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

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:

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:

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:

Analytes to measure: Levonorgestrel and ethinyl estradiol in plasma.

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

Recommended Nov 2009
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.