

Draft Guidance on Ethinyl Estradiol; Norgestrel

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way, crossover *in-vivo*
Strength: 0.05 mg/0.5 mg
Subjects: Healthy nonpregnant females, general population
Additional Comments: Subjects should not be taking hormonal contraceptives

2. Type of study: Fed
Design: Single-dose, two-way, crossover *in-vivo*
Strength: 0.05 mg/0.5 mg
Subjects: Healthy nonpregnant females, general population
Additional comments: Please see comment above

Analytes to measure: Ethinyl estradiol and norgestrel in plasma

Bioequivalence based on (90% CI): Ethinyl estradiol and norgestrel

Waiver request of in-vivo testing: Not Applicable

Referencing/Cross-referencing of *in-vivo* testing: For the lower strength, 0.03 mg/0.3 mg EE/NG submitted in a separate ANDA, based on (1) acceptable bioequivalence studies of the 0.05 mg/0.5 mg EE/NG strength from a separate but related ANDA, (2) cross-referencing of the studies above in the separate ANDA of the 0.03 mg/0.5 mg EE/NG strength (3) acceptable in vitro dissolution testing of both strengths, and (3) proportional similarity of the formulations between two strengths.

If only the lower strength, 0.03 mg/0.3 mg EE/NG, 21-day regimen or 28-day regimen, is to be marketed first, the fasting and fed studies should be conducted on this lower strength, comparing it with the equal strength of the reference product of the same bundle (linked to the current guidance). In such case, if later the higher strength, 0.05 mg/0.5 mg EE/NG 21 or 28-day regimen is to be marketed, an **additional** fasting study will be requested for this higher strength of 21 or 28-day regimen, without cross-referencing of the studies of the lower strength.

Please note that if different NDA/ANDAs of Ethinyl Estradiol and Norgestrel Tablets, 0.03 mg/0.3 mg and 0.05 mg/0.5 mg are referenced, separate applications must be submitted. Please refer to the Guidance for Industry, *Variations in Drug Products that May Be Included in a Single ANDA* located at: <http://www.fda.gov/cder/guidance>.

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.