Contains Nonbinding Recommendations

Draft Guidance on Ethinyl Estradiol; Norethindrone

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

Active Ingredient: Ethinyl estradiol; Norethindrone

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in vivo
   Strength: 0.05 mg/1 mg
   Subjects: Healthy nonpregnant females, general population
   Additional comments: None

---

2. Type of study: Fed
   Design: Single-dose, two-way crossover in vivo
   Strength: 0.05 mg/1 mg
   Subjects: Healthy nonpregnant females, general population
   Additional comments: None

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/0.4 mg strengths based on (i) acceptable bioequivalence studies on the 0.05 mg/1 mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths

Note that when referencing different reference products of ethinyl estradiol and norethindrone tablets, as designated in the reference listed drug (RLD) application number column, separate applications should be submitted. Refer to the guidance for industry *Variations in Drug Products that May be Included in a Single ANDA* at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072892.pdf

If a sponsor intends to develop and market only the lower strength, 0.035 mg/0.4 mg, then the studies recommended above comparing 0.035 mg/0.4 mg strength to the corresponding strength of the reference product should be conducted. If, following conduct of the studies with the lower

strength, the sponsor intends to develop and market the higher strength, 0.05 mg/1 mg, an additional fasting study with this strength should be conducted.

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods Web site, available to the public at the following location: http://www.accessdata.fda.gov/scripts/cder/dissolution/. 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 abbreviated new drug application (ANDA).