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Draft Guidance on Ethinyl Estradiol; Norethindrone Acetate

August 2022

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This guidance, which interprets the Agency’s regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

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In July 2014, FDA issued a draft product-specific guidance for industry on generic ethinyl estradiol; norethindrone acetate. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

Active Ingredients: Ethinyl estradiol; Norethindrone acetate

Dosage Form; Route: Tablet; oral

Recommended Studies: Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 0.02 mg; 1 mg
Subjects: Non-pregnant, non-lactating females, general population
Additional comment: The tablet should be swallowed whole with 240 mL of water.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 0.02 mg; 1 mg
Subjects: Non-pregnant, non-lactating females, general population
Additional comment: See comment above.

Analytes to measure: Ethinyl estradiol and norethindrone in plasma

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

Waiver request of in vivo testing: Not applicable

Dissolution test method and sampling times: The dissolution information for this drug product can be found in the FDA's Dissolution Methods database, <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Conduct comparative dissolution testing on 12 dosage units for each of the test and reference products. Specifications will be determined upon evaluation of the ANDA.

Revision History: Recommended July 2014; Revised August 2022

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