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Draft Guidance on Ethinyl Estradiol; Norgestimate

October 2024

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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.

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Active Ingredients: Ethinyl estradiol; Norgestimate

Dosage Form: Tablet

Route: Oral-21, Oral-28

Strengths: 0.025 mg; 0.18 mg, 0.025 mg; 0.215 mg, 0.025 mg; 0.25 mg, 0.035 mg; 0.18 mg, 0.035 mg; 0.215 mg, 0.035 mg; 0.25 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 0.035 mg; 0.25 mg
   Subjects: Healthy non-pregnant, non-lactating females
   Additional comments: None

Analytes to measure: Ethinyl estradiol and 17-desacetyl norgestimate in plasma

Bioequivalence based on (90% CI): Ethinyl estradiol and 17-desacetyl norgestimate

Waiver request of in vivo testing: 0.025 mg; 0.18 mg, 0.025 mg; 0.215 mg, 0.025 mg; 0.25 mg, 0.035 mg; 0.180 mg, and 0.035 mg; 0.215 mg strengths, based on (i) acceptable bioequivalence study on the 0.035 mg; 0.25 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths

Cross-referencing of in vivo testing:
Note that ethinyl estradiol and norgestimate tablets, 0.025 mg; 0.18 mg, 0.025 mg; 0.215 mg, 0.025 mg; 0.25 mg, 0.035 mg; 0.18 mg, 0.035 mg; 0.25 mg, and 0.035 mg; 0.215 mg are the subject of three separate reference listed drugs (RLDs). Three separate abbreviated new drug applications (ANDA) must be submitted comparing to the appropriate RLDs. An applicant may request a waiver of in vivo bioequivalence testing for generic of these RLDs provided that it (1) submits an ANDA containing acceptable bioequivalence study on the 0.035 mg; 0.25 mg strength; (2) cross-references the ANDA for the 0.035 mg; 0.25 mg strength; and (3) meets the criteria of 21 CFR § 320.22(d)(2). Refer to the most recent version of the FDA guidance for industry on *Variations in Drug Products that May Be Included in a Single ANDA*.[a]

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 all strengths of the test product and RLD.[1] Specifications will be determined upon review of the ANDA.

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[a] For the most recent version of a guidance, check the FDA guidance website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[1] If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions.*