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Draft Guidance on Loperamide Hydrochloride; Simethicone

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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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This is a new draft product-specific guidance for industry on generic loperamide hydrochloride; simethicone.

Active Ingredients: Loperamide hydrochloride; Simethicone

Dosage Form; Route: Tablet, chewable; oral

Recommended Studies: Two in vivo bioequivalence studies with pharmacokinetic endpoints and one in vitro defoaming study

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 2 mg; 125 mg
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comment: The tablet should be chewed, then swallowed with water.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 2 mg; 125 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comment: See comment above.

3. Type of study: In vitro
Conduct the U.S. Pharmacopeia (USP) in vitro defoaming study to measure the functional ability of simethicone to collapse bubbles produced by a foaming soap solution (1 g octoxynol-9/100 mL water). To demonstrate bioequivalence for the simethicone component, the following intro tests should be conducted: a) the USP in vitro defoaming testing, and b) the modified USP in vitro defoaming testing, wherein whole tablets are used instead of crushed tablets. The specification is a clear solution within 30 seconds.

Analyte to measure: Loperamide in plasma

Bioequivalence based on (90% CI): Loperamide

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 each of the test and reference products. Specifications will be determined upon review of the ANDA.

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