Contains Nonbinding Recommendations

Draft Guidance on Loperamide Hydrochloride; Simethicone

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended Studies: One in vivo study and one in vitro study

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in vivo
   Strength: 2 mg/125 mg at a dose of 4 mg/ 250 mg (2 x 2 mg/ 125 mg)
   Subjects: Healthy males and nonpregnant females, general population
   Additional comments: None

2. Type of study: In vitro

   Conduct the U.S. Pharmacopeia (USP) in vitro defoaming test to measure the functional ability of simethicone to collapse bubbles produced by a foaming soap solution (1 gram 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.

Analytes to measure (in appropriate biological fluid): 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 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).