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Draft Guidance on Lansoprazole

November 2021

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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.

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in FDA guidances means that something is suggested or recommended, but not required.

In February 2018, FDA issued a draft product-specific guidance for industry on generic lansoprazole. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

Active Ingredient: Lansoprazole

Dosage Form; Route: Tablet, orally disintegrating, delayed release; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 30 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: The orally disintegrating tablet should be placed on the tongue, allowed to disintegrate, and swallowed without water. Applicants may consider using a reference-scaled average bioequivalence approach for lansoprazole. If using this approach, provide evidence of high variability in the pharmacokinetic parameters (i.e., within-subject variability $\geq 30\%$) for the reference product. For detailed information on this approach, refer to the product-specific guidance on *Progesterone, Capsule; Oral*.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 30 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: See comments above

Analyte to measure: Lansoprazole in plasma

Bioequivalence based on (90% CI): Lansoprazole

Additional Strength: Bioequivalence of the 15 mg strength to the corresponding reference product strength may be demonstrated based on principles described in the FDA guidance on *Bioequivalence Studies With Pharmacokinetic Endpoints for Drugs Submitted Under an ANDA*.

Dissolution test method and sampling times: For modified release drug products, applicants should develop specific discriminating dissolution methods. Alternatively, applicants may use the dissolution method set forth in any related official United States Pharmacopeia (USP) drug product monograph, or in the FDA's database, <http://www.accessdata.fda.gov/scripts/cder/dissolution/>, provided that applicants submit adequate dissolution data supporting the discriminating ability of such a method. If a new dissolution method is developed, submit the dissolution method development and validation report with the complete information/data supporting the proposed method. Conduct comparative dissolution testing on 12 dosage units for each strength of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.

Product-specific testing conditions for in vitro feeding tube studies: The approved labeling for the reference product states that the product may be administered by a nasogastric (NG) tube (8 French or greater). Conduct the in vitro feeding tube studies including comparative recovery testing with three repeated administrations, particle size distribution study, comparative acid resistance stability testing, and sedimentation volume testing. For general procedures of in vitro feeding tube studies, refer to the FDA guidance on *Oral Drug Products Administered Via Enteral Feeding Tube: In Vitro Testing and Labeling Recommendations*.

Testing tube: NG tube (8 French)

Testing strengths: 15 mg, 30 mg

Dispersion medium: 15 mg strength in 4 mL and 30 mg strength in 10 mL water with different pH values (e.g., pH 5.5, 7.0 and 8.5)

Testing conditions for acid resistance stability testing: 500 mL of 0.1 N HCl maintained at $37 \pm 0.5^\circ\text{C}$; USP Apparatus II at 75 rpm. Analyze the amount of lansoprazole released at 60 minutes

Incubation times: 0 and 15 minutes

Revision History: Recommended October 2008; Revised July 2009, June 2016,
October 2016, February 2018, November 2021

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