

Draft Guidance on Dexlansoprazole

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Delayed-release orally disintegrating tablets; 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: Applicants may consider using a reference-scaled average bioequivalence approach. For the method of statistical analysis using the reference-scaled average bioequivalence approach, refer to the Progesterone Capsule Guidance.

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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.

Analytes to measure (in appropriate biological fluid): Dexlansoprazole in plasma

Bioequivalence based on (90% CI): Dexlansoprazole

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 the test and reference products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).

Alcohol Dose Dumping Studies:

Due to a concern of dose dumping of drug from this drug product when taken with alcohol, the

Agency currently requests that additional dissolution testing be conducted using various concentrations of ethanol in the dissolution medium, as follows:

Testing Conditions: Volume: 500 mL 0.1N HCl, USP apparatus 1 (basket) @100 rpm, with and without alcohol:

Test 1: Twelve units tested according to the proposed method, with data collected every 15 minutes for a total of 2 hours

Test 2: Twelve units analyzed by substituting 5% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours

Test 3: Twelve units analyzed by substituting 20% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours

Test 4: Twelve units analyzed by substituting 40% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours

After completion of the acid stage testing, each sample should be transferred to the corresponding buffer stage medium containing the same level of ethanol as the acid stage. The pH of the buffer media should be adjusted to pH 7.2 after adding the ethanol.

Testing Conditions: Volume: 900 mL 50 mmol/L phosphate buffer (pH 7.20) containing 5 mmol/L sodium lauryl sulfate, USP apparatus 1 (basket) @100 rpm, with and without alcohol.

Both test and RLD products must be tested accordingly and data must be provided on individual unit, means, range and %CV on all strengths.

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, particle size distribution study, comparative acid resistance stability testing, and sedimentation volume testing. Refer to the Lansoprazole Delayed-Release Orally Disintegrating Tablet Draft Guidance for additional information regarding procedures of in vitro feeding tube studies.

Testing tube: NG tube (8 French)

Testing strength: 30 mg

Dispersion medium: 20 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 I at 100 rpm. Analyze the amount of dexlansoprazole released at 120 minutes.