

Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Posaconazole

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

In general, FDA’s guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency’s current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredient: Posaconazole

Dosage Form: Tablet, delayed release

Route: Oral

Strength: 100 mg

Recommended Studies: Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 100 mg
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of posaconazole. Alternatively, a parallel study design may be considered.
2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 100 mg
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: See comments above.

Analyte to measure: Posaconazole in plasma

Bioequivalence based on (90% CI): Posaconazole

Additional strengths: Not applicable

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

Alcohol dose dumping studies: Due to concerns of dose dumping of drug from this product when taken with alcohol, conduct additional dissolution testing using various concentrations of ethanol in the dissolution medium as follows:

Testing conditions: 900 mL, 0.1 N HCl, USP Apparatus 2 (paddle) at 100 rpm, with or without alcohol

Test 1: 12 units tested according to the proposed method (with 0.1 N HCl) with data collected every 15 minutes for a total of 2 hours

Test 2: 12 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: 12 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: 12 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

Conduct testing on both test and RLD products accordingly, and provide data on individual unit, means, range and %CV.

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