

Draft Guidance on Posaconazole

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind the FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active Ingredient: Posaconazole

Dosage Form; Route: Delayed release tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in vivo
Strength: 100 mg
Dose: 100 mg
Subjects: Healthy males and non-pregnant females, general population.
Additional comments: Females should not be lactating, and, if applicable, should practice abstinence or contraception during the study.

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2. Type of study: Fed
Design: Single-dose, two-way crossover in vivo
Strength: 100 mg
Dose: 100 mg
Subjects: Healthy males and non-pregnant females, general population.
Additional comments: See comments above.
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Analytes to measure (in appropriate biological fluid): Posaconazole in plasma

Bioequivalence based on (90% CI): Posaconazole

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 website 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).

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: 900 mL, 0.1 N HCl, USP apparatus 2 (paddle) @50 rpm, with and without the alcohol (see below):

Test 1: 12 units tested according to the proposed method (with 0.1N 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

Both test and reference listed drug (RLD) products must be tested accordingly and data must be provided on individual unit, means, range and %CV on both strengths.