Contains Nonbinding Recommendations

Draft Guidance on Clonazepam

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Orally disintegrating tablets; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single dose, two-way crossover in vivo
   Strength: 1 mg
   Subjects: Healthy males and females (nonpregnant), general population.
   Additional Comments: The orally disintegrating tablet should be placed on the tongue and allowed to disintegrate without water. Applicants should include a urine toxicology test in the study protocol to prevent concomitant opioid use with clonazepam orally disintegrating tablet.

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2. Type of study: Fed
   Design: Single dose, two-way crossover in vivo
   Strength: 1 mg
   Subjects: Healthy males and females (nonpregnant), general population.
   Additional Comments: Please see comments above.

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

Bioequivalence based on (90% CI): Clonazepam

Waiver request of in vivo testing: 0.125 mg, 0.25 mg, 0.5 mg, and 2 mg based on (i) acceptable bioequivalence studies on the 1 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulation across all strengths.

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).