

Draft Guidance on Clobazam

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Film; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 20 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of clobazam, alternatively, a parallel study design may be considered. Follow the “Instruction for Use” carefully in the reference listed drug labels, place drug on top of the tongue, close mouth and swallow saliva normally as drug dissolves, but not take with liquids and not chew, spit or talk while drug dissolves.

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2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 20 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: See comments above
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Analytes to measure: Clobazam and its active metabolite, N-desmethyloclobazam, in plasma

Bioequivalence based on (90% CI): Clobazam

Submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max} .

Waiver request of in vivo testing: 5 mg and 10 mg strengths based on (i) acceptable bioequivalence studies on the 20 mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths

Dissolution test method and sampling times: The dissolution information for this drug product can be found in the FDA's Dissolution Methods database, <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Conduct comparative dissolution testing on 12 dosage units for each of all strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.