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Draft – Not for Implementation

Draft Guidance on Diazepam

May 2025

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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Active Ingredient: Diazepam

Dosage Form: Film

Route: Buccal

Strengths: 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 10 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: The buccal film should be placed on the inside of the cheek and allowed to dissolve without water. Do not administer with liquids. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of diazepam. Alternatively, a parallel study design may be considered. Subjects should be evaluated prior to discharge for cognitive impairment such as drowsiness, dizziness, and confusion and instructed not to drive or operate machinery until their cognitive function returns to baseline level. A lower strength of 10 mg is recommended based on the central nervous system depressive effects which may occur at higher incidence rate with higher doses.

Analyte to measure: Diazepam in plasma

Bioequivalence based on (90% CI): Diazepam

Waiver request of in vivo testing: 5 mg, 7.5 mg, 12.5 mg, and 15 mg strengths based on (i) an acceptable bioequivalence study on the 10 mg strength, (ii) acceptable in vitro dissolution testing of all the strengths, and (iii) proportional similarity of the formulations across 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 product and reference listed drug (RLD).[1] Specifications will be determined upon evaluation of the abbreviated new drug application.

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Unique Agency Identifier: PSG_218623

[1] If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions.*