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Draft Guidance on Zonisamide

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form: Capsule

Route: Oral

Strengths: 25 mg, 50 mg, 100 mg, 150 mg,[1] 200 mg,[1] 300 mg[1]

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: 300 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments:
   - Females of reproductive potential should have a negative pregnancy test within 24 hours prior to receiving the drug. Females of reproductive potential should use non-hormonal contraception during the study and continue to use effective contraception for one month after the last dose. $AUC_{(0\text{-}72h)}$ may be used in place of $AUC_{(0\text{-}t)}$ when comparing the extent of absorption, due to zonisamide's long half-life. Ensure an adequate washout period between treatments in the crossover study. Alternatively, a parallel study design may be considered.
   - Exclude subjects with a history of drug hypersensitivity. Subjects should be evaluated prior to discharge for cognitive impairment and instructed not to drive or operate machinery until their cognitive function returns to baseline level.

[1] Strengths identified are the subject of an approved suitability petition (FDA-2018-P-0098).

Applicants may consider one of the following approaches which is appropriate at time of the study:

- Conduct the study by testing one zonisamide capsule (1 × 300 mg) of the test drug product compared to three zonisamide capsules (3 × 100 mg) of the reference standard (RS), when applicants use the reference listed drug (RLD), NDA 020789, zonisamide capsules, 100 mg as the RS.
- Alternatively, applicants may conduct the study by testing one zonisamide capsule (1 × 300 mg) of the test drug product compared to one zonisamide capsule (1 × 300 mg) of the RS, when there is an approved petitioned abbreviated new drug application (ANDA) for zonisamide capsules, 300 mg, which is designated as the RS.

Analyte to measure: Zonisamide in plasma

Bioequivalence based on (90% CI): Zonisamide

Waiver request of in vivo testing: 25 mg, 50 mg, 100 mg, 150 mg and 200 mg strengths based on (i) acceptable bioequivalence study on the 300 mg strength, (ii) acceptable in vitro dissolution testing of all 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).[2] Specifications will be determined upon review of the ANDA.

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[2] 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*.