Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Zuranolone

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredient: Zuranolone

Dosage Form: Capsule

Route: Oral

Strengths: 20 mg, 25 mg, 30 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 30 mg
   Subjects: Healthy non-pregnant, non-lactating females
   Additional comments: Exclude geriatric subjects. Female subjects of reproductive potential should use non-hormonal contraception during the study and continue to use effective contraception for one week after the last dose. Subjects should be evaluated prior to discharge for cognitive impairment such as sedation and confusion and instructed not to drive or operate machinery until their cognitive function returns to baseline level.

Analyte to measure: Zuranolone in plasma

Bioequivalence based on (90% CI): Zuranolone

Waiver request of in vivo testing: 20 mg and 25 mg strengths based on (i) an acceptable bioequivalence study on the 30 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).[1] Specifications will be determined upon review of the abbreviated new drug application.

Document History: Recommended May 2025

Unique Agency Identifier: PSG_217369

[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*.