Contains Nonbinding Recommendations

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Draft Guidance on Zolpidem Tartrate

August 2026

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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: Zolpidem tartrate

Dosage Form: Tablet

Route: Sublingual

Strengths: 1.75 mg | 3.5 mg

Reference Listed Drug: NDA 022328

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Class of study: Bioequivalence
   Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 3.5 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Safety recommendations:
   - Exclude geriatric subjects due to increased risk of impaired motor/cognitive performance and unusual sensitivity to sedative/hypnotic drugs.
   - Subjects should be evaluated prior to discharge for cognitive impairment such as drowsiness and instructed not to drive or operate machinery until their cognitive function returns to baseline level.

   Study design recommendation:
   - Place the tablet under the tongue and allow it to disintegrate completely before swallowing; do not swallow the tablet whole.

Analyte to measure: Zolpidem in plasma

Bioequivalence based on (90% CI): Zolpidem

Bioequivalence of additional strengths: Waiver request of in vivo testing of additional strength based on (i) an acceptable bioequivalence study on the 3.5 mg strength, (ii) acceptable comparative in vitro dissolution studies between the additional strength and the 3.5 mg strength using 12 units per strength, and (iii) proportional similarity of the formulations across both strengths

Dissolution: Dissolution test(s) should be included for quality control and to support a waiver request of in vivo testing of additional strength. For the quality control dissolution method, provide a dissolution method development report for the test product containing information and data that demonstrate appropriateness of the selected dissolution method[1] and sampling times, such as the discriminating ability to detect changes in critical quality attributes that could potentially impact drug product performance.

Document History: Recommended June 2012; Revised August 2026

[1] Applicant-developed, United States Pharmacopeia drug product monograph or Dissolution Methods database, https://www.accessdata.fda.gov/scripts/cder/dissolution/index.cfm