

Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Zolpidem Tartrate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:	5 mg 10 mg
Reference Listed Drug:	NDA 021997
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: 10 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; do not swallow the tablet whole and do not take with water.

Analyte to measure: Zolpidem in plasma

Bioequivalence based on (90% CI): Zolpidem

Bioequivalence of additional strength: Waiver request of in vivo testing of additional strength based on (i) an acceptable bioequivalence study on the 10 mg strength, (ii) acceptable comparative in vitro dissolution studies between the additional strength and the 10 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 method¹ 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 September 2010; 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>