

Draft Guidance on Zolpidem Tartrate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Zolpidem Tartrate

Form/Route: Spray; Oral

Recommended studies: 2 options: In vivo or In vitro

I. In Vivo Option:

If the test product is **not** qualitatively (Q1) and quantitatively (Q2) the same as the reference product, the following study is recommended to document bioequivalence of the test product to the reference product:

1. Type of study: Fasting
Design: Single-dose, two-way crossover in-vivo
Strength: 5 mg/spray x 1 spray (5 mg dose)
Subjects: Healthy males and non-regnant females, general population.
Additional Comments: Subjects should be advised not to drive if they are experiencing drowsiness and/or dizziness at the end of the study

Analytes to measure (in appropriate biological fluid): Zolpidem in plasma

Bioequivalence based on (90% CI): Zolpidem

Waiver request of in-vivo testing: Not Applicable

Dissolution test method and sampling times: Not Applicable

Additional information: While comparative in vitro studies are not required, in vitro studies outlined in the 2002 Guidance for Industry, *Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products – Chemistry, Manufacturing, and Controls Documentation* (<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070575.pdf>) should be submitted for Chemistry, Manufacturing, and Controls evaluation.

II. In Vitro Option:

If the test product is qualitatively (Q1) and quantitatively (Q2) the same as the reference product, then bioequivalence may be documented by an in vitro approach in lieu of an in vivo approach.

Equivalent in vitro performance of the test product to the reference product should be established. The current FDA recommendations for documenting equivalent spray device performance via in vitro testing may be found in the draft guidance “Bioavailability and Bioequivalence Studies for Nasal Aerosols and Nasal Sprays for Local Action”. The guidance is available at

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070111.pdf> under Biopharmaceutics Draft (April 2003).