

Contains Nonbinding Recommendations

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Draft Guidance on Acetaminophen; Tramadol Hydrochloride

October 2024

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Active Ingredients: Acetaminophen; Tramadol hydrochloride

Dosage Form: Tablet

Route: Oral

Strength: 325 mg; 37.5 mg

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: 325 mg; 37.5 mg
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: Acetaminophen; tramadol hydrochloride tablet is under a Risk Evaluation and Mitigation Strategy (REMS) with Elements to Assure Safe Use (ETASU). All pertinent elements of the REMS/ETASU are recommended to be incorporated into the protocol and informed consent.

Analytes to measure: Tramadol using an achiral assay and acetaminophen in plasma

Bioequivalence based on (90% CI): Acetaminophen and tramadol

Waiver request of in vivo testing: Not applicable

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 the test product and reference listed drug (RLD).¹ Specifications will be determined upon review of the abbreviated new drug application.

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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*.