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Draft Guidance on Tapentadol Hydrochloride

October 2024

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Active Ingredient:	Tapentadol hydrochloride
Dosage Form:	Tablet
Route:	Oral
Strengths:	50 mg, 75 mg, 100 mg
Recommended Studies:	Two options: (1) Biopharmaceutics Classification System (BCS)-based biowaiver or (2) one in vivo bioequivalence study with pharmacokinetic endpoints

I. Option 1: BCS Class I-based biowaiver

A waiver request of in vivo testing for all the strengths of this product may be considered provided that the appropriate documentation regarding high solubility, high permeability and rapid dissolution as detailed in the most recent version of the FDA guidance for industry on *M9 Biopharmaceutics Classification System-Based Biowaivers*[a] is submitted in the application. Applicants may use the information contained in the approved labeling of the reference listed drug (RLD). Peer reviewed articles may not contain the necessary details of the testing for the Agency to make a judgment regarding the quality of the studies. A decision regarding the acceptability of the waiver request can only be made upon assessment of the data submitted in the application.

Option 2: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 100 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Tapentadol 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.

Analyte to measure: Tapentadol in plasma

Bioequivalence based on (90% CI): Tapentadol

Waiver request of in vivo testing: 50 and 75 mg strengths based on (i) an acceptable bioequivalence study on the 100 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 RLD.[1] Specifications will be determined upon review of the abbreviated new drug application.

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[a] For the most recent version of a guidance, check the FDA guidance website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[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.*