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Draft Guidance on Sibutramine Hydrochloride

October 2024

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Active Ingredient: Sibutramine hydrochloride

Dosage Form: Capsule

Route: Oral

Strengths: 5 mg, 10 mg, 15 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: 15 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Due to safety concerns, studies should not be conducted using doses higher than 15 mg.

Analytes to measure: Sibutramine, and the major first-generation active (desmethyl) metabolites M1 and M2, using an achiral assay

Bioequivalence based on (90% CI): Sibutramine

If sibutramine can be reliably measured, a confidence interval approach for bioequivalence determination should be used for sibutramine. If sibutramine cannot be reliably measured, a confidence interval approach for bioequivalence determination should be used for major first-generation active (desmethyl) metabolites M1 and M2.

Waiver request of in vivo testing: 5 mg and 10 mg based on (i) acceptable bioequivalence study on the 15 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 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.*