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Draft Guidance on Isosorbide Dinitrate

October 2024

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Active Ingredient: Isosorbide dinitrate

Dosage Form: Tablet

Route: Oral

Strengths: 5 mg, 10 mg, 20 mg, 30 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: 30 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: None

Analytes to measure: Isosorbide dinitrate, isosorbide-5-mononitrate, and isosorbide-2-mononitrate in plasma

Submit data for isosorbide dinitrate's active metabolites (isosorbide-5-mononitrate and isosorbide-2-mononitrate) as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}.

Bioequivalence based on (90% CI): Isosorbide dinitrate

Waiver request of in vivo testing: 5 mg, 10 mg, and 20 mg strengths based on (i) acceptable bioequivalence study on the 30 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*.