

Draft Guidance on Isosorbide Dinitrate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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: Isosorbide dinitrate

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in vivo
Strength: 30 mg
Subjects: Healthy males and nonpregnant females, general population
Additional comments: Not applicable (N/A)
2. Type of study: Fed
Design: Single-dose, two-way crossover in vivo
Strength: 30 mg
Subjects: Healthy males and nonpregnant females, general population
Additional comments: N/A

Analytes to measure (in appropriate biological fluid): 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 based on (i) acceptable bioequivalence studies on the 30 mg strength, (ii) proportional similarity across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods website available to the public at the following location:

<http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products.

Specifications will be determined upon review of the abbreviated new drug application (ANDA).