

Contains Nonbinding Recommendations

Draft Guidance on Nitroglycerin

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Sublingual Tablet/Oral

Recommended study: 1 study

1. Type of study: Fasting
Design: Single-dose, two-way crossover in-vivo
Strength: 0.6 mg base
Subjects: Healthy males and nonpregnant females, general population
Additional comments: Applicants may consider using a reference-scaled average bioequivalence approach for nitroglycerin and its metabolites. If using this approach, please provide evidence of high variability in the bioequivalence parameters of AUC and/or C_{max} (i.e., within-subject variability $\geq 30\%$). Please refer to the Progesterone Capsule Guidance for additional information regarding highly variable drugs.

Analytes to measure (in appropriate biological fluid): Nitroglycerin and its active metabolites, 1,2-dinitroglycerin and 1,3-dinitroglycerin, in plasma.

Bioequivalence based on (90% CI): Nitroglycerin

Please submit the metabolite data 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} .

Waiver request of in-vivo testing: 0.3 mg and 0.4 mg based on (i) acceptable bioequivalence study on the 0.6 mg strength, (ii) acceptable in-vitro dissolution testing of all strengths, and (iii) proportional similarity in the formulations across all strengths. Please refer to the Mirtazapine Tablet Draft Guidance for additional information regarding waivers of in-vivo testing.

Dissolution test method and sampling times:

Please note that a Dissolution Methods Database is available to the public at the OGD website at <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Please find the dissolution information for this product at this website. Please 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 application.