

Draft Guidance on Nitroglycerin

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

Active Ingredient: Nitroglycerin

Dosage Form; Route: Powder; sublingual

Recommended Studies: One study

1. Type of study: Fasting
Design: Single-dose, two-way crossover in-vivo
Strength: 0.4 mg/packet at the dose of 0.8 mg (2 x 0.4 mg)
Subjects: Healthy males and non-pregnant, non-lactating females, general population.
Additional Comments: (1) Product labeling states that the dose may be administered under the tongue. Sublingual administration is recommended for the bioequivalence study. (2) Applicants may consider using a reference-scaled average bioequivalence approach for nitroglycerin. If using this approach, please provide, from the fasting study, 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 Bioequivalence Recommendations for Specific Products Guidance on Progesterone Capsules for additional information regarding this approach.

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: Not Applicable

Dissolution test method and sampling times: Not Applicable