Contains Nonbinding Recommendations

Draft Guidance on Nitroglycerin

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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: Ointment; transdermal

Recommended Studies: One study

Type of study: Fasting
Design: Single-dose, two-way, crossover in vivo
Strength: 2%
Subjects: Healthy males and nonpregnant females, general population
Additional comments: Approximately ½ inch or 375 mg of nitroglycerin ointment, 2%, containing 7.5 mg of nitroglycerin should be dosed, as recommended in the reference listed drug (RLD) label, using an applicator to evenly cover the same skin surface area for the test and reference products. Application of the ointment should be randomized to one side of the torso for the RLD in one study period and to the contralateral side of the torso for the test product in the other study period.

Heart rate and blood pressure should be monitored throughout the study. Applicants may consider using a reference-scaled average bioequivalence (BE) approach for nitroglycerin. If using this approach, provide evidence of high variability in the BE parameters of AUC and/or C_{max} (i.e., within-subject variability $\geq 30\%$). Refer to the BE 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

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 (AUC, C_{max} and T_{max}); and geometric means and ratios of means for AUC and C_{max}

Waiver request of in vivo testing: Not applicable (N/A)

Dissolution test method and sampling times: N/A