

Guidance on Disulfiram

This guidance represents 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: Disulfiram

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover *in-vivo*
Strength: 500 mg
Subjects: Healthy males and nonpregnant females, general population
Additional Comments: none

2. Type of study: Fed
Design: Single-dose, two-way crossover *in-vivo*
Strength: 500 mg
Subjects: Healthy males and nonpregnant females, general population
Additional comments: none

Analytes to measure (in appropriate biological fluid): Disulfiram and its active metabolites N,N-diethylthiocarbamate (DDC) and S-methyl N,N-diethylthiocarbamate (MeDDC) in plasma

Please submit the metabolite data as supporting 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): Disulfiram

If disulfiram can be reliably measured, please analyze the data for the parent compound using the confidence interval approach. The data for the active metabolites can be used as supportive evidence. However, if you can demonstrate that it is not possible to measure disulfiram in plasma accurately and reliably, please analyze the primary metabolite DDC using the confidence interval approach. If you demonstrate the DDC in plasma cannot be reliably and accurately measured, please analyze the secondary metabolite MeDDC using the confidence interval approach.

Waiver request of in-vivo testing: 250 mg based on (i) acceptable bioequivalence studies on the 500 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 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).