

Draft Guidance on Trametinib dimethyl sulfoxide

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended Studies: One study

1. Type of study: Fasting, pharmacokinetic endpoint steady state
Design: Multiple-dose, two-way crossover
Strength: 2 mg (trametinib) tablet (dose=2 mg daily until steady state)
Subjects: The study should be conducted in patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test.
Additional Comments: 1) Attainment of steady state should be confirmed with at least three consecutive trough levels. 2) Blood sampling for bioequivalence should consist of appropriate sampling times over a 24-hour period following attainment of steady state. 3) Investigators should refer to Warnings, Precautions, Contraindications, and Adverse Reactions in the FDA-approved labeling and follow the recommendations closely. 4) The study should be designed around each patient's existing Trametinib regimen and no changes in dose or regimen should be made for the purpose of the bioequivalence study.

Analytes to measure (in appropriate biological fluid): Trametinib in plasma

Bioequivalence based on (90% CI): Trametinib

Waiver request of in vivo testing: 0.5 mg and 1 mg strength tablets, based on (i) acceptable bioequivalence study on the 2 mg strength, (ii) proportional similarity in formulations 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 Web site, 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.