

Draft Guidance on Vemurafenib

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended Study: One study

Type of study: Pharmacokinetic steady state study

Design: Multiple dose, two-way cross-over in patients for whom the drug is clinically indicated

Strength: 240 mg tablet (dose=4x240 mg=960 mg twice daily)

Study Subjects: The study should be conducted in patients with BRAF V600E mutation- positive metastatic melanoma.

Additional Comments: 1) Attainment of steady state should be confirmed with at least 3 consecutive trough levels; 2) Blood sampling for bioequivalence should consist of appropriate sampling times over a 12-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 Vemurafenib 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): Vemurafenib in plasma

Bioequivalence based on (90% CI): Vemurafenib

Waiver request of in-vivo testing: N/A

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).