Contains Nonbinding Recommendations

Draft Guidance on Dabrafenib Mesylate

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Capsule; oral

Recommended Studies: One in vivo study

1. Type of study: Fasting
   Design: Multiple-dose, steady-state, two-way crossover in vivo
   Strength: EQ 75mg base at a dose of 150 mg (2x EQ 75 mg base)
   Subjects: Patients already receiving a stable dose of dabrafenib mesylate tablets
   Additional comments:
   a. Patients should be confirmed to have the BRAF V600E mutation in tumor specimens, as detected by an FDA-approved test, prior to initiation of treatment with Tafinlar® as a single agent.
   b. Tafinlar® may cause hemolytic anemia in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency. Subjects should be screened for the G6PD deficiency prior to their enrollment.
   c. Females should not be pregnant or lactating, and, if applicable, should practice abstention or contraception during the study.

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

Bioequivalence based on (90% CI): Dabrafenib

Waiver request of in vivo testing: EQ 50 mg base based on (i) acceptable bioequivalence study on the EQ 75 mg base strength, (ii) proportionally similar formulation 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 (ANDA).