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Draft Guidance on Trametinib Dimethyl Sulfoxide

May 2022

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

This guidance, which interprets the Agency's regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

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In January 2016, FDA issued a draft product-specific guidance for industry on generic trametinib dimethyl sulfoxide. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

Active Ingredient: Trametinib dimethyl sulfoxide

Dosage Form; Route: Tablet; oral

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: EQ 2 mg Base
   Subjects: Healthy males and females not of reproductive potential
   Additional comments: Subjects with a history of, or current evidence of, either central serous retinopathy or retinal vein thrombosis, or both, or any risk factors for these conditions, including uncontrolled glaucoma or a history of hyper viscosity or hyper coagulability syndromes, should be excluded from the bioequivalence study. Male subjects (including those who have had vasectomies) with female partners of

reproductive potential should use condoms throughout the study and for at least 4 months after the last dose.

Analyte to measure: Trametinib in plasma

Bioequivalence based on (90% CI): Trametinib

Waiver request of in vivo testing: EQ 0.5 mg Base and EQ 1 mg Base strengths based on (i) acceptable bioequivalence study on the EQ 2 mg Base 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 in the FDA's Dissolution Methods database, 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 ANDA.

Revision History: Recommended January 2016; Revised May 2022

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