Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Crizotinib

October 2024

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredient: Crizotinib

Dosage Form: Capsule

Route: Oral

Strengths: 200 mg, 250 mg

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: 250 mg
   Subjects: Healthy males and healthy females not of reproductive potential
   Additional comments: Exclude subjects >70 years of age. Exclude subjects with hypertension or cardiovascular risk factors. Monitor liver function tests, electrocardiogram, urinalysis, and vital signs prior to dosing and after each dosing period. Males with female partners of reproductive potential should use condoms during the study and for at least 90 days after the last dose.

Analyte to measure: Crizotinib in plasma

Bioequivalence based on (90% CI): Crizotinib

Waiver request of in vivo testing: 200 mg strength based on (i) an acceptable bioequivalence study on the 250 mg strength, (ii) acceptable in vitro dissolution testing of both strengths, and (iii) proportional similarity of the formulations between both 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 for each of both strengths of the test product and reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

Document History: Recommended July 2014; Revised October 2024

Unique Agency Identifier: PSG_202570

[1] If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions*.