Contains Nonbinding Recommendations

Draft Guidance on Brigatinib

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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:	Brigatinib
Dosage Form; Route:	Tablet; oral
Recommended studies:	One study

Type of study: Steady State
Design: Multiple Dose, crossover *in-vivo*
Strength: 180 mg
Subjects: Patients with established dosing regimen who are receiving a stable dose of 180 mg brigatinib tablets

Additional Comments: Recruitment efforts should be targeted at patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotini, and who are on an established dosing regimen of 180mg brigatinib tablets.

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

Bioequivalence based on (90% CI): Brigatinib

In the evaluation of the steady-state bioequivalence study, the following pharmacokinetics data should be submitted for Brigatinib: $AUC_{0\text{-}tau}$, and C_{maxSS}. In addition, report C_{minSS} (concentration at the end of a dosing interval), C_{avSS} (average concentration during a dosing interval), degree of fluctuation [$(C_{max\text{-}Cmin})/C_{avSS}$], swing [$(C_{maxSS}\text{-}C_{minSS})/C_{minSS}$], and T_{max}.

Waiver request of in-vivo testing: 30 mg and 90 mg base based on (i) acceptable bioequivalence study on the 180 mg 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 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.