

Draft Guidance on Alpelisib

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 200 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: 1) Exclude subjects with risk factors for prolonged QTc interval and Torsades de Pointes; 2) Monitor subjects during the study for electrocardiogram changes and laboratory values; 3) Females of reproductive potential and males with female partners of reproductive potential should use effective contraception during the study and one week after the last dose of alpelisib.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 200 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: See comments above

Analyte to measure: Alpelisib in plasma

Bioequivalence based on (90% CI): Alpelisib

Waiver request of in vivo testing: The 50 mg and 150 mg strengths based on (i) acceptable bioequivalence studies on the 200 mg strength, (ii) proportional similarity of the formulations 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 for each of all strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.