

Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Alpelisib

February 2026

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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: Alpelisib

Dosage Form: Tablet

Route: Oral

Strengths: 50 mg, 125 mg, 200 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 200 mg
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: Exclude subjects with risk factors for prolonged QTc interval and Torsades de Pointes. Exclude subjects with a history of drug hypersensitivity to prevent severe cutaneous adverse reactions. Females of reproductive potential should use effective contraception during the study and for one week after the last dose. Males with female partners of reproductive potential should use condoms and effective contraception during the study and one week after the last dose.

Analyte to measure: Alpelisib in plasma

Bioequivalence based on (90% CI): Alpelisib

Waiver request of in vivo testing: An applicant may request a waiver of in vivo bioequivalence testing, if the applicant cross-references an approved abbreviated new drug application for alpelisib tablets, 50 mg, 150 mg, 200 mg referencing NDA 212526.

Waiver request of in vivo testing of additional strength: Justification based on (i) an acceptable bioequivalence study on the 200 mg strength, (ii) acceptable comparative in vitro dissolution studies between additional strengths and the 200 mg strength using 12 units per strength, and (iii) proportional similarity of the formulations across all strengths

Dissolution: Dissolution tests should be included for quality control and to support waiver request of in vivo testing of additional strengths.

Dissolution test method and sampling times: Provide a dissolution method development report for the test product containing information and data that demonstrate appropriateness of the selected dissolution method and sampling times, such as the discriminating ability to detect changes in critical quality attributes that could potentially impact drug product performance.

Product-specific testing conditions for in vitro feeding tube studies: The approved labeling for the reference listed drug states that the product may be administered by a nasogastric (NG) or gastrostomy (G) tube. Conduct the in vitro feeding tube studies, including comparative recovery, sedimentation volume and redispersibility testing, and in-use stability in designated dispersion media, and particle size distribution study. For general procedures of in vitro feeding tube studies, refer to the most recent version of the guidance for industry *Oral Drug Products Administered Via Enteral Feeding Tube: In Vitro Testing and Labeling Recommendations*.^a

Testing tube: NG tube (5 French) and G tube (12 French)

1. Comparative recovery testing
 - Three different configurations of 5 French NG tubes, defined by materials (e.g., polyvinylchloride, silicone, polyurethane) and/or designs (e.g., number of ports/eyes, open or closed distal end), including:
 - One configuration made of polyurethane
 - One configuration made of silicone
 - One additional configuration
 - Three different configurations of 12 French G tubes, including:
 - One configuration made of silicone
 - Two additional configurations
 - At least one tube should be tested with an inflated balloon design
 - Reporting of the pH value of the water
 - Holding times of 0 and 60 minutes
2. Sedimentation volume and redispersibility testing
3. In-use stability testing
4. Particle size distribution study

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Unique Agency Identifier: PSG_215039

^a For the most recent version of a guidance, refer to the FDA guidance website at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>.