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Draft Guidance on Ibrutinib

August 2024

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Active Ingredient: Ibrutinib

Dosage Form: Tablet

Route: Oral

Strengths: 140 mg, 280 mg, 420 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: 420 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Due to the embryo-fetal toxicity of ibrutinib, female subjects of reproductive potential should use effective method of contraception during the study and for one month after the last dose. Males with female partner of reproductive potential should use effective method of contraception during the study and for one month after the last dose. Applicants may consider using a reference-scaled average bioequivalence approach for ibrutinib. If using this approach, provide evidence of high variability in the pharmacokinetic parameters (i.e., within-subject variability ≥30%) for the reference listed drug. For detailed information on this approach, refer to the most recent version of the FDA guidance for industry on *Bioequivalence Studies with Pharmacokinetic Endpoints for Drugs Submitted Under an ANDA*.[a]

Analyte to measure: Ibrutinib in plasma

Bioequivalence based on (90% CI): Ibrutinib

Waiver request of in vivo testing: 140 mg, and 280 mg strengths based on (i) acceptable bioequivalence study on the 420 mg 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 abbreviated new drug application.

Revision History: Recommended September 2019; Revised August 2024

Unique Agency Identifier: PSG_210563

[a] For the most recent version of a guidance, check the FDA guidance website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.