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Draft Guidance on Cabozantinib S-Malate

May 2023

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Active Ingredient: Cabozantinib S-malate

Dosage Form; Route: Capsule; Oral

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: EQ 80 mg Base
   Subjects: Healthy males not of reproductive potential (i.e., surgically sterile) and healthy females not of reproductive potential
   Additional comments: Exclude subjects with abnormal liver function tests. Exclude subjects who have undergone or plan to undergo any surgery or dental procedure for at least 2 weeks prior to the study and at least 3 weeks after the last dose. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of cabozantinib. Alternatively, a parallel study design may be considered.

Analyte to measure: Cabozantinib in plasma

Bioequivalence based on (90% CI): Cabozantinib

Waiver request of in vivo testing: EQ 20 mg Base strength based on (i) acceptable bioequivalence study on the EQ 80 Base 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 and reference products. Specifications will be determined upon review of the abbreviated new drug application.

Revision History: Recommended February 2018; Revised May 2023

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