Draft Guidance on Cabozantinib S-Malate

May 2023

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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: 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

Contains Nonbinding Recommendations
Draft - Not for Implementation

Recommended Feb 2018; Revised May 2023
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

Unique Agency Identifier: PSG_203756