

Draft Guidance on Lenvatinib Mesylate

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Capsule; Oral

Recommended Studies: Two in vivo studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in-vivo
Strength: EQ 10 mg Base
Subjects: Healthy males and females (non-pregnant and non-lactating), general population.
Additional Comments:
 - 1) Lenvatinib has a long elimination half-life. FDA recommends ensuring an adequate washout period is used in the crossover study design. Alternatively, a parallel study design is recommended if the crossover study design is problematic. For long half-life drug products, an AUC truncated to 72 hours may be used in place of AUC_{0-t} or AUC_{0-inf} if the drug demonstrates low intra-subject variability in distribution and clearance.
 - 2) Lenvatinib can cause fetal harm. Female subjects should not be pregnant or lactating, and should practice abstinence or contraception during the study and for at least two weeks thereafter. In addition, general toxicology studies suggest the potential for lenvatinib to impair fertility at sub-therapeutic exposures in males and females of reproductive potential.

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2. Type of study: Fed
Design: Single-dose, two-way crossover in-vivo
Strength: EQ 10 mg Base
Subjects: Healthy males and females (non-pregnant and non-lactating), general population.
Additional Comments: See comments above.

Analytes to measure (in appropriate biological fluid): Lenvatinib in plasma

Bioequivalence based on (90% CI): Lenvatinib

Waiver request of in vivo testing: EQ 4 mg Base strength based on (I) acceptable bioequivalence studies on the EQ 10 mg Base strength, (II) proportional similar 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 website available to the public at the following location: <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 (ANDA).