

Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Lenvatinib Mesylate

November 2024

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|---------------------------|-----------------------------------------------------------------|
| Active Ingredient: | Lenvatinib mesylate |
| Dosage Form: | Capsule |
| Route: | Oral |
| Strengths: | EQ 4 mg Base, EQ 10 mg Base |
| 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 10 mg Base
Subjects: Healthy males and healthy females not of reproductive potential
Additional comments: Exclude subjects with abnormal liver function tests or blood pressure. Exclude subjects who have undergone or plan to undergo elective surgery including dental procedures for at least two weeks prior to and at least one week after taking the study drug. Male subjects with female partners of reproductive potential should use effective contraception during the study and for at least two weeks after the last dose. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of lenvatinib. Alternatively, a parallel study design may be considered.

Analyte to measure: Lenvatinib in plasma

Bioequivalence based on (90% CI): Lenvatinib

Waiver request of in vivo testing: EQ 4 mg Base strength based on (i) an acceptable bioequivalence study on the EQ 10 mg 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 product and reference listed drug (RLD).¹ Specifications will be determined upon review of the abbreviated new drug application.

Product-specific testing conditions for in vitro feeding tube studies: The approved labeling for the RLD states that lenvatinib suspension can be administered via feeding tubes with water. The labeling instruction on preparing suspension is to place the required number of capsules in a small container with 20 mL water. In vitro nasogastric (NG) tube and gastrostomy (G) tube studies are recommended including comparative recovery, sedimentation volume and redispersibility, 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 FDA guidance for industry, *Oral Drug Products Administered Via Enteral Feeding Tube: In Vitro Testing and Labeling Recommendations*.^a

Testing tube:

- NG tube
 - 5 French tubes with polyvinyl chloride and polyurethane materials
 - 6 French tubes with silicone material
- G tube
 - 12 French tubes different materials(e.g., polyvinyl chloride, silicone, polyurethane) and/or different designs (e.g., number of ports and/or eyes, open or closed distal end, retention balloons)
 - 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 24 hours

Sedimentation volume and redispersibility testing

In-use stability in designated dispersion media (i.e., water)

Particle size distribution study

¹ If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions*.

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