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Draft Guidance on Osimertinib Mesylate

October 2024

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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Active Ingredient: Osimertinib mesylate

Dosage Form: Tablet

Route: Oral

Strengths: EQ 40 mg Base, EQ 80 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 80 mg Base
   Subjects: Healthy males and healthy females not of reproductive potential
   Additional comments: Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of osimertinib. Alternatively, a parallel study design may be considered. Males with female partners of reproductive potential to use effective contraception during the study and for 4 months after the last dose.

Analyte to measure: Osimertinib in plasma

Bioequivalence based on (90% CI): Osimertinib

Waiver request of in vivo testing: EQ 40 mg Base strength based on (i) acceptable bioequivalence study on the EQ 80 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 reference product states that the product may be administered via a nasogastric (NG) tube. Conduct the in vitro feeding tube studies including comparative recovery testing and sedimentation volume and redispersibility testing. For general procedures of in vitro feeding tube studies, refer to the most recent version of the FDA guidance for industry on *Oral Drug Products Administered Via Enteral Feeding Tube: In Vitro Testing and Labeling Recommendations*.[a]

Testing tube: NG tube (8 French)

Testing strength: EQ 80 mg Base

Dispersion medium: EQ 80 mg Base strength in 50 mL water with pH >7

Incubation times: 0 and 15 minutes

Document History: Recommended October 2017; Revised February 2022, October 2024

Unique Agency Identifier: PSG_208065

[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

[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*.