*Contains Nonbinding Recommendations*

*Draft – Not for Implementation*

# Draft Guidance on Quizartinib Dihydrochloride

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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.

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**Active Ingredient:** Quizartinib dihydrochloride

**Dosage Form:** Tablet

**Route:** Oral

**Strengths:** EQ 17.7 mg Base, EQ 26.5 mg Base

**Recommended Studies:** Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: EQ 26.5 mg Base
   Subjects: Healthy males and healthy females not of reproductive potential
   Additional comments: Exclude subjects with QTc interval >450 milliseconds, risk factors or history of Torsades de Pointes, long QT syndrome, or ventricular arrhythmias. Exclude subjects with abnormal electrolyte levels. Monitor electrocardiograms during the study. Males with female partners of reproductive potential should use effective contraception during the study and for four months after the last dose. Quizartinib is under a Risk Evaluation and Mitigation Strategy (REMS) with Elements to Assure Safe Use (ETASU), which restricts its use. All pertinent elements of the REMS/ETASU must be incorporated into the protocol and informed consent. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of quizartinib and its active metabolite, AC886. Alternatively, a parallel study design may be considered.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: EQ 26.5 mg Base
Subjects: Healthy males and healthy females not of reproductive potential
Additional comments: See comments above.

**Analytes to measure:** Quizartinib and its active metabolite, AC886, in plasma

Submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and $C_{max}$.

**Bioequivalence based on (90% CI):** Quizartinib

**Waiver request of in vivo testing:** EQ 17.7 mg Base strength based on (i) acceptable bioequivalence studies on the EQ 26.5 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.

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**Document History:** Recommended November 2024

**Unique Agency Identifier:** PSG_216993

[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.*