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Draft Guidance on Revumenib Citrate

December 2025

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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:	Revumenib citrate
Dosage Form:	Tablet
Route:	Oral
Strengths:	EQ 25 mg Base, EQ 110 mg Base, EQ 160 mg Base
Recommended Studies:	Two options: (1) one in vivo bioequivalence study with pharmacokinetic endpoints, or (2) alternative approach to establish bioequivalence

I. Option 1: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Steady-state
   Design: Multiple-dose, two-treatment, two-period crossover in vivo
   Strength: EQ 160 mg Base
   Subjects: Male and female patients with relapsed or refractory acute leukemia with a lysine methyltransferase 2A gene translocation who are receiving a stable dose of revumenib citrate tablets based on the approved indications
   Additional comments: Exclude patients who may require dosage modification or who expect changes in concomitant medications that may potentially affect the pharmacokinetics of revumenib during the study. Female patients of reproductive potential should use effective contraception during treatment and for 4 months after the last dose. Male patients of reproductive potential should use effective contraception during treatment and for 4 months after the last dose. Implement safety precautions and monitoring including complete blood count during treatment as recommended in the labeling. Patients should be instructed to take the drug under similar food conditions during both periods of the study.

Analyte to measure: Revumenib in plasma

Bioequivalence based on (90% CI): Revumenib

II. Option 2: Alternative approach to establish bioequivalence

Revumenib may be eligible for a Biopharmaceutics Classification System (BCS) class III-based biowaiver. A waiver request of in vivo testing for all the strengths of this product may be considered provided that the appropriate documentation regarding high solubility, very rapid dissolution of the test product and reference listed drug (RLD)[a], and the test product formulation is qualitatively the same and quantitatively very similar as detailed in the most recent version of the FDA guidance for industry *M9 Biopharmaceutics Classification System-Based Biowaivers*[a] is submitted in the application. Applicants may use the information contained in the approved labeling of the RLD. Peer-reviewed articles may not contain the necessary details of the testing for the Agency to make a judgement regarding the quality of the studies. A decision regarding the acceptability of the waiver request can only be made upon assessment of the data submitted in the application.

Waiver request of in vivo testing: EQ 25 mg Base and EQ 110 mg Base strengths based on (i) an acceptable bioequivalence study on the EQ 160 mg Base strength, (ii) acceptable in vitro dissolution testing across all strengths, and (iii) proportional similarity of the formulations across all 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 each of all strengths of the test product and RLD.[1] Specifications will be determined upon review of the abbreviated new drug application.

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[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 guidance for industry *Referencing Approved Drug Products in ANDA Submissions*.