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Draft Guidance on Ruxolitinib Phosphate

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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:	Ruxolitinib phosphate
Dosage Form:	Tablet
Route:	Oral
Strengths:	EQ 5 mg Base, EQ 10 mg Base, EQ 15 mg Base, EQ 20 mg Base, EQ 25 mg Base
Recommended Studies:	Two options: (1) Biopharmaceutics Classification System (BCS)-based biowaiver or (2) one in vivo bioequivalence study with pharmacokinetic endpoints

I. Option 1: BCS Class I-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, high permeability and rapid dissolution as detailed in the most recent version of the FDA guidance for industry on *M9 Biopharmaceutics Classification System-Based Biowaivers*[a] is submitted in the application. Applicants may use the information contained in the approved labeling of the reference listed drug (RLD). Peer reviewed articles may not contain the necessary details of the testing for the Agency to make a judgment 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.

II. Option 2: 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 25 mg Base
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: None

Analyte to measure: Ruxolitinib in plasma

Bioequivalence based on (90% CI): Ruxolitinib

Waiver request of in vivo testing: EQ 5 mg Base, EQ 10 mg Base, EQ 15 mg Base, and EQ 20 mg Base strengths based on (i) acceptable bioequivalence study on the EQ 25 mg Base strength, (ii) acceptable in vitro dissolution testing of 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 for each of all strengths of the test product and RLD.[1] Specifications will be determined upon review of the abbreviated new drug application.

In vitro feeding tube studies should be conducted for both aforementioned options (BCS Class I-based biowaiver option and in vivo bioequivalence study with pharmacokinetic endpoints option).

Testing tube: NG tube (8 French)

Testing strengths: EQ 5 mg Base and EQ 25 mg Base

Dispersion media: Water with different pH values (e.g., pH 5.5, 7.0 and 8.5)

Incubation times: 0 minute and 6 hours

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