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Draft Guidance on Ruxolitinib Phosphate

February 2022

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

This guidance, which interprets the Agency's regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

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In January 2017, FDA issued a draft product-specific guidance for industry on generic ruxolitinib phosphate. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

Active Ingredient: Ruxolitinib phosphate

Dosage Form; Route: Tablet; oral

Recommended Studies: Two options: Biopharmaceutics Classification System (BCS) based biowaiver or in vivo bioequivalence studies

I. BCS Class I-based biowaiver option:

A waiver request of in vivo testing for 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 abbreviated new drug application (ANDA). Applicants may use information contained in the approved labeling of the reference product. Peer-reviewed articles may not contain the necessary details of the testing for the FDA to make a judgment regarding the quality

of the studies. A decision regarding the acceptability of the waiver request will be made upon assessing the data submitted in the ANDA.

II. In vivo bioequivalence study option:

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

2. Type of study: Fed
   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 studies on the EQ 25 mg Base strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations in 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 and reference products. Specifications will be determined upon review of the ANDA.

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 (8 French or greater). Conduct the in vitro feeding tube studies including comparative recovery testing with repeated administrations, 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]

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

Revision History: Recommended September 2015; Revised December 2016, January 2017, February 2022

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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