

Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Apixaban

February 2022

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 We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

Active Ingredient: Apixaban

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 5 mg
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: 5 mg
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: None

Analyte to measure: Apixaban in plasma

Bioequivalence based on (90% CI): Apixaban

Waiver request of in vivo testing: 2.5 mg strength based on (i) acceptable bioequivalence studies on the 5 mg 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 and reference products. 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 by 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: 5 mg

Dispersion media: 1. 60 mL of water; 2. 60 mL of 5% dextrose in water

Incubation times: 0 and 15 minutes

Revision History: Recommended June 2013; Revised May 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>