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Draft Guidance on Baricitinib

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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: Baricitinib

Dosage Form; Route: Tablet; oral

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: 4 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Exclude subjects with latent tuberculosis, abnormal liver function tests or blood counts, or at an increased risk for thrombosis. Do not use live attenuated vaccines immediately prior to or during the study.

2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 4 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: See comments above.

Analyte to measure: Baricitinib in plasma

Bioequivalence based on (90% CI): Baricitinib

Waiver request of in vivo testing: 1 mg and 2 mg strengths based on (i) acceptable bioequivalence studies on the 4 mg 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 and reference products. Specifications will be determined upon review of the Abbreviated New Drug Application (ANDA).

Product-specific testing conditions for in vitro feeding tube studies:
Since the approved labeling for the reference product states that the product may be administered via a feeding tube, in vitro nasogastric (NG) tube/orogastric (OG) tube and gastrostomy (G) tube studies are recommended which include comparative recovery, sedimentation volume, and re-dispersibility.

Testing tubes: NG/OG tube (8 French) and G tube (12 French) with different tube materials (e.g., polyvinyl chloride, silicone, polyurethane) and/or designs (e.g., various numbers of ports and/or eyes, retention balloons, open or closed distal end). At least one G tube should be tested with an inflated balloon design.

Testing strengths: 1 mg, 2 mg, and 4 mg

Dispersion and rinse medium: Dispersed a tablet with 30 mL of water for NG/OG tube or 15 mL of water for G tube. Flush remaining contents from NG/OG or G tubes with 15 mL of water. Report the pH value of the water.

Holding times: 0 and 15 minutes

Revision History: Recommended September 2019; Revised November 2022

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