Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Allopurinol

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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: Allopurinol

Dosage Form: Suspension[1]

Route: Oral

Strength: 100 mg/5 mL

Recommended Studies: Two options: (1) two in vivo bioequivalence studies with pharmacokinetic endpoints using the designated reference standard (RS) for allopurinol tablets, or (2) one in vivo bioequivalence study with pharmacokinetic endpoints using the designated RS for allopurinol suspension

I. Option 1: Two in vivo bioequivalence studies with pharmacokinetic endpoints using the designated RS for allopurinol tablets[2]

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 100 mg/5 mL at a dose of 300 mg (15 mL)
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Conduct the study comparing a test suspension of 100 mg/5 mL at a dose of 300 mg (15 mL) to a 300 mg tablet of the RS.

[1] Dosage form identified is the subject of approved suitability petitions (FDA-2008-P-0209 and FDA-2011-P-0740).
[2] The currently designated RS for allopurinol tablets is the abbreviated new drug application (ANDA), ANDA 211820, allopurinol tablets, 300 mg.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 100 mg/5 mL at a dose of 300 mg (15 mL)
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: See comments above.

II. Option 2: One in vivo bioequivalence study with pharmacokinetic endpoints using the designated RS for allopurinol suspension[3]

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 100 mg/5 mL at a dose of 300 mg (15 mL)
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: An additional bioequivalence study under fed conditions may be necessary if allopurinol suspension is deemed high-risk. High-risk products are those where the drug substance characteristics in combination with the complexity of the formulation design or manufacturing process lead to an increased likelihood that in vivo performance may be impacted differently by varying gastrointestinal conditions between the fasted and fed conditions. Refer to the most recent version of the FDA guidance for industry on *M13A Bioequivalence for Immediate-Release Solid Oral Dosage Forms*.[4]

Analyte to measure: Allopurinol in plasma

Bioequivalence based on (90% CI): Allopurinol

Waiver request of in vivo testing: Not applicable

Dissolution test method and sampling times: The dissolution information for the RS 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 the test product and the RS. Specifications will be determined upon review of the abbreviated new drug application.

Document History: Recommended November 2024

Unique Agency Identifier: PSG_016084-Sus

[3] This option can be used when a petitioned ANDA for allopurinol suspension is approved and designated as the RS. There is currently no approved petitioned ANDA for allopurinol suspension.
[4] https://www.fda.gov/media/165049/download