

Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Metolazone

October 2024

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Active Ingredient: Metolazone

Dosage Form: Tablet

Route: Oral

Strengths: 2.5 mg, 5 mg, 10 mg

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: 10 mg
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: None
2. 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

Analyte to measure: Metolazone in plasma

Bioequivalence based on (90% CI): Metolazone

Waiver request of in vivo testing: 2.5 mg strength based on (i) acceptable bioequivalence studies on the 5 mg and 10 mg strengths, (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 reference listed drug (RLD).¹ Specifications will be determined upon review of the abbreviated new drug application.

Document History: Recommended November 2010; Revised October 2024

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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*.