Contains Nonbinding Recommendations

Draft Guidance on Empagliflozin and Metformin Hydrochloride

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Active Ingredient: Empagliflozin and Metformin Hydrochloride

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: 12.5 mg (Empagliflozin)/1000 mg (Metformin Hydrochloride)
   Subjects: Healthy males, and non-pregnant females, general population.
   Additional Comments: To avoid hypoglycemic episodes in healthy volunteers, the drug products should be administered with 240 mL of a 20% glucose solution in water, followed by 60 mL of the glucose solution administered every 15 min for up to 4 hours after dosing.

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2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover *in-vivo*
   Strength: 12.5 mg (Empagliflozin)/1000 mg (Metformin Hydrochloride)
   Subjects: Healthy males, and non-pregnant females, general population.
   Additional comments: See comment above

Analytes to measure (in appropriate biological fluid): Empagliflozin and Metformin

Bioequivalence based on (90% CI): Empagliflozin and Metformin

Waiver request of in-vivo testing: The 12.5 mg/500 mg, 5 mg/1000 mg and 5 mg/500 mg strengths based on i) the acceptable bioequivalence studies on the 12.5 mg/1000 mg strength, ii) proportional similarity of formulations across all strengths and iii) acceptable in vitro dissolution testing of all strengths.

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods website available to the public at the following location: 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 abbreviated new drug application (ANDA).