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Draft Guidance on Empagliflozin; Linagliptin

October 2024

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Active Ingredients: Empagliflozin; Linagliptin

Dosage Form: Tablet

Route: Oral

Strengths: 10 mg; 5 mg, 25 mg; 5mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 25 mg; 5 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments:
   a. Females of reproductive potential should use effective contraception during the study.
   b. The drug product should be administered with 240 mL of a 20% glucose solution in water, followed by 60 mL of the glucose solution administered every 15 minutes for up to 4 hours after dosing. Monitor blood glucose concentrations and signs and symptoms of hypoglycemia during the study. Implement appropriate hypoglycemia management protocol.
   c. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of linagliptin. Alternatively, a parallel study design may be considered.

Analytes to measure: Empagliflozin and linagliptin in plasma

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

Waiver request of in vivo testing: 10 mg; 5 mg strength based on (i) acceptable bioequivalence study on the 25 mg; 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 product and reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

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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*.