Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Empagliflozin; Metformin Hydrochloride

October 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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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 Ingredients: Empagliflozin; Metformin hydrochloride

Dosage Form: Tablet

Route: Oral

Strengths: 5 mg; 500 mg, 5 mg; 1 gm, 12.5 mg; 500 mg, 12.5 mg; 1 gm

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 12.5 mg; 1 gm
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: 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.

Analytes to measure: Empagliflozin and metformin

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

Waiver request of in vivo testing: 5 mg; 500 mg, 5 mg; 1 gm, and 12.5 mg; 500 mg strengths based on (i) the acceptable bioequivalence study on the 12.5 mg; 1 gm 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 product and reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

Document History: Recommended June 2016; Revised October 2024

Unique Agency Identifier: PSG_206111

[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*.