Draft Guidance on Dapagliflozin; Saxagliptin Hydrochloride

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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 Ingredients: Dapagliflozin; Saxagliptin 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: 10 mg; EQ 5 mg Base
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: To avoid hypoglycemic episodes, 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 minutes for up to 4 hours after dosing.

2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 10 mg; EQ 5 mg Base
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: See comments above

Analytes to measure (in appropriate biological fluid): Dapagliflozin, saxagliptin and its active metabolite, 5-hydroxy saxagliptin, in plasma

Submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and Cmax.

Bioequivalence based on (90% CI): Dapagliflozin and saxagliptin

Waiver request of in vivo testing: The 5 mg; EQ 5 mg Base strength based on (i) acceptable bioequivalence studies on the 10 mg; EQ 5 mg Base strength, (ii) proportional similarity of the formulations between both strengths, and (iii) acceptable in vitro dissolution testing of both strengths.

Recommended Sep 2018; Revised Jun 2020
**Dissolution test method and sampling times:** The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods web site, available to the public at the following location: [http://www.accessdata.fda.gov/scripts/cder/dissolution/](http://www.accessdata.fda.gov/scripts/cder/dissolution/). Conduct comparative dissolution testing on 12 dosage units for each strength of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.