Contains Nonbinding Recommendations

Draft Guidance on Dapagliflozin; Saxagliptin Hydrochloride

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.

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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

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/. 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.