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Draft Guidance on Alogliptin Benzoate; Pioglitazone Hydrochloride

October 2024

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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: Alogliptin benzoate; Pioglitazone hydrochloride

Dosage Form: Tablet

Route: Oral

Strengths: EQ 12.5 mg Base; EQ 15 mg Base,
EQ 12.5 mg Base; EQ 30 mg Base,
EQ 12.5 mg Base; EQ 45 mg Base,
EQ 25 mg Base; EQ 15 mg Base,
EQ 25 mg Base; EQ 30 mg Base,
EQ 25 mg Base; EQ 45 mg Base

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: EQ 25 mg Base; EQ 45 mg Base
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Females of reproductive potential should use effective contraception during the study. 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: Alogliptin and pioglitazone and pioglitazone metabolite M-IV 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 C_{max}.

Bioequivalence based on (90% CI): Alogliptin and pioglitazone

Waiver request of in vivo testing: EQ 12.5 mg Base; EQ 15 mg Base, EQ 12.5 mg Base; EQ 30 mg Base, EQ 12.5 mg Base; EQ 45 mg Base, EQ 25 mg Base; EQ 15 mg Base, and EQ 25 mg Base; EQ 30 mg Base, strengths based on (i) acceptable bioequivalence study on the EQ 25 mg Base; EQ 45 mg Base 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.

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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.*