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Draft Guidance on Pioglitazone Hydrochloride

October 2024

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Active Ingredient: Pioglitazone hydrochloride

Dosage Form: Tablet

Route: Oral

Strengths: EQ 15 mg Base, EQ 30 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 45 mg Base
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Monitor blood glucose concentrations and signs and symptoms of hypoglycemia during the study. Implement appropriate hypoglycemia management protocol.

Analytes to measure: Pioglitazone and its active metabolite, M-IV in plasma

Bioequivalence based on (90% CI): Pioglitazone

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}.

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