Contains Nonbinding Recommendations

Draft Guidance on Pioglitazone Hydrochloride

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Pioglitazone Hydrochloride

Form/Route: Tablet/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: Eq 45 mg base
   Subjects: Healthy males and nonpregnant females, general population.
   Additional Comments: To avoid hypoglycemic episodes in healthy volunteers, 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 min for up to 4 hours after dosing.

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2. Type of study: Fed
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: Eq 45 mg base
   Subjects: Healthy males and nonpregnant females, general population.
   Additional Comments: Please see comment above

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

Bioequivalence based on (90% CI): Pioglitazone

Please submit the metabolite M-IV 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.

Waiver request of in-vivo testing: Eq 15 mg base and Eq 30 mg base, based on (i) acceptable bioequivalence studies 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:

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at: http://www.accessdata.fda.gov/scripts/cder/dissolution/. Please find the dissolution information for this product at this website. Please conduct comparative dissolution testing on 12 dosage units each of the test and reference products. Specifications will be determined upon review of the application.