Contains Nonbinding Recommendations

Draft Guidance on Glyburide; Metformin Hydrochloride

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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 ingredients: Glyburide; Metformin Hydrochloride

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in-vivo
   Strength: 2.5 mg/500 mg
   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.

2. Type of study: Fed
   Design: Single-dose, two-way crossover in-vivo
   Strength: 2.5 mg/500 mg
   Subjects: Healthy males and nonpregnant females, general population
   Additional Comments: Please see comment above.

Analytes to measure (in appropriate biological fluid): Glyburide and metformin in plasma

Bioequivalence based on (90% CI): Glyburide and metformin

Waiver request of in-vivo testing: 1.25 mg/250 mg and 5 mg/500 mg based on (i) acceptable bioequivalence studies on the 2.5 mg/500 mg strength, (ii) acceptable in vitro dissolution testing across all strengths, and (iii) proportional similarity in 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 all strengths of the test and reference products. Specifications will be determined upon review of the application.

Finalized May 2008; Revised Dec 2009