Contains Nonbinding Recommendations

Draft Guidance on Glimepiride and Rosiglitazone Maleate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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: Glimepiride/Rosiglitazone Maleate

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover *in-vivo*
   Strength: 1 mg/4 mg
   Subjects: Normal healthy males and females, general population. Females must have a negative baseline pregnancy test within 24 hours prior to receiving the drug. Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study.
   Additional Comments: Because of the potential for hypoglycemia from BE studies using the 4 mg dose of glimepiride tablets, in vivo BE study of the 1 mg glimepiride/4 mg rosiglitazone maleate tablets is recommended. In addition, each dose in the study should be administered with 240 mL of 20% glucose solution to minimize hypoglycemic effects. After dosing, 60 mL of 20% glucose solution should be given to each subject every 15 min for the following 4 hours

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2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover *in-vivo*
   Strength: 1 mg/4 mg
   Subjects: Normal healthy males and females, general population. Females must have a negative baseline pregnancy test within 24 hours prior to receiving the drug. Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study.
   Additional Comments: Please see Additional Comments above.

Analytes to measure (in appropriate biological fluid): Glimepiride and Rosiglitazone in plasma.

Bioequivalence based on (90% CI): Glimepiride and Rosiglitazone

Waiver request of in-vivo testing: 2 mg/4 mg; 4 mg/4 mg; 2 mg/8 mg; and 4 mg/8 mg tablets, based on acceptable (i) bioequivalence studies on the 1 mg/4 mg tablet, and (ii) proportional similarity of the formulations and (iii) acceptable in vitro dissolution testing of 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.fda.gov/cder/ogd/index.htm. 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.