Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Glimepiride; Rosiglitazone Maleate

October 2024

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

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: Glimepiride; Rosiglitazone maleate

Dosage Form: Tablet

Route: Oral

Strengths: 1 mg; 4 mg, 2 mg; 4 mg, 2 mg; 8 mg, 4 mg; 4 mg, 4 mg; 8 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 1 mg; 4 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Females must have a negative baseline pregnancy test within 24 hours prior to receiving the drug. 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: Glimepiride and rosiglitazone in plasma

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

Waiver request of in vivo testing: 2 mg; 4 mg, 2 mg; 8 mg, 4 mg; 4 mg, and 4 mg; 8 mg strengths based on (i) acceptable bioequivalence study on the 1 mg; 4 mg 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.

Document History: Recommended November 2007; Revised October 2024

Unique Agency Identifier: PSG_021700

[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*.