Contains Nonbinding Recommendations

Draft Guidance on Flutamide

Active ingredient: Flutamide

Form/Route: Capsules; Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in vivo
   Strength: 125 mg x 2 capsules (250 mg dose)
   Subjects: Healthy males
   Additional Comments:

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2. Type of study: Fed
   Design: Single-dose, two-way crossover in vivo
   Strength: 125 mg x 2 capsules (250 mg dose)
   Subjects: Healthy males
   Additional Comments:

Analytes to measure: Flutamide and active metabolite, hydroxyflutamide in plasma

Bioequivalence based on (90% CI): Flutamide and hydroxyflutamide

Please use flutamide plasma concentrations for bioequivalence determination and analyze the flutamide AUC and Cmax data using the confidence interval approach if its plasma concentrations can be reliably measured and its pharmacokinetic parameters accurately determined. The data for the active metabolite hydroxyflutamide can be used to provide 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.

If it is not possible to measure flutamide in plasma accurately and reliably, then the bioequivalence determination will be based on the hydroxyflutamide AUC and Cmax data, which will be analyzed using the confidence interval approach.

Waiver request of in vivo testing: Not Applicable

Dissolution test method and sampling times:

Please note tat 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.