Contains Nonbinding Recommendations

Draft Guidance on Mifepristone

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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.

Active Ingredient: Mifepristone

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 300 mg
   Subjects: Males and postmenopausal females, general population
   Additional comments: Specific recommendations are provided below

---

2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 300 mg
   Subjects: Males and postmenopausal females, general population
   Additional comments: Specific recommendations are provided below

---

Analytes to measure (in appropriate biological fluid): Mifepristone and its two primary metabolites, N-monodemethylated (RU 42 633) and hydroxylated (RU 42 698)

Bioequivalence based on (90% CI): mifepristone

Submit data for the two primary metabolites of mifepristone, N-monodemethylated (RU 42 633) and hydroxylated (RU 42 698), as supportive evidence of comparable therapeutic outcome. The following data should be submitted for the metabolites: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}.

Waiver request of in vivo testing: Not applicable

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods Web site, available to the public at the following location: http://www.accessdata.fda.gov/scripts/cder/dissolution/. Conduct comparative dissolution testing on 12 dosage units for each strength of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.

Additional Comments: Due to the anti-gestational effects of mifepristone, the studies should be conducted in males and postmenopausal females. “Postmenopausal” is defined as 12 months of spontaneous amenorrhea or 6 months of spontaneous amenorrhea with serum follicle stimulating hormone (FSH) levels > 40 mIU/ml or at least 6 weeks postsurgical following bilateral oophorectomy with or without hysterectomy.

To ensure that the bioequivalence studies incorporate the appropriate safeguards against exposure to the drug, the Agency recommends that study protocols incorporate safety measures including:

> Providing a Korlym® Medication Guide to all subjects and only enrolling subjects who are able to read the Medication Guide either in English or in a provided translation.