Draft Guidance on Mifepristone

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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: 200 mg
   Subjects: Males and postmenopausal females, general population
   Additional comments:
   a) Mifeprex (mifepristone) Tablets are approved with a Risk Evaluation and Mitigation Strategy (REMS) with Elements to Assure Safe Use (ETASU), which restricts its use. Incorporate all pertinent elements of the REMS into the protocol and informed consent, including putting processes and procedures in place to maintain a distribution system that is secure and confidential and follows all processes and procedures, including those for storage, handling, shipping, tracking, and controlled returns of study drug.
   b) Specific recommendations are provided below

2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 200 mg
   Subjects: Males and postmenopausal females, general population
   Additional comments: See comments above

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

Bioequivalence based on (90% CI): Mifepristone

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

**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/](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.

**Specific recommendations:** Due to the anti-gestational effects of mifepristone, both bioequivalence studies should be conducted in males and postmenopausal females, general population. “Postmenopausal” is defined as 12 months of spontaneous amenorrhea or 6 months of spontaneous amenorrhea with serum follicle-stimulating hormone (FSH) concentrations > 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 Mifeprex® 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.