

## Guidance on Diclofenac Sodium; Misoprostol

This guidance represents 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:** Diclofenac Sodium; Misoprostol

**Form/Route:** Delayed Tablets/Oral

**Recommended studies:** 2 studies

1. Type of study: Fasting  
Design: Single-dose, two-way crossover *in-vivo*  
Strength: 75 mg/0.2 mg  
Subjects: Normal healthy males and females, general population  
Additional Comments: Female subjects should be excluded from the bioequivalence study if they are pregnant.

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2. Type of study: Fed  
Design: Single-dose, two-way crossover *in-vivo*  
Strength: 75 mg/0.2 mg  
Subjects: Normal healthy males and females, general population  
Additional comments: Female subjects should be excluded from the bioequivalence study if they are pregnant.

**Analytes to measure:** Diclofenac and misoprostol's metabolite, misoprostol acid in plasma.

**Bioequivalence based on (90% CI):** Diclofenac and misoprostol's metabolite, misoprostol acid. Please submit the metabolite data as 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.

**Waiver request of in-vivo testing:** 50 mg/ 0.2 mg based on (i) acceptable bioequivalence studies on the 75 mg/0.2 mg strength, (ii) proportional similarity of the formulations across all strengths, 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.