Contains Nonbinding Recommendations

Draft Guidance on Diclofenac Sodium

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Delayed Release Tablets/Oral

Recommended studies: 4 studies

1. Type of study: Fasting
   Design: Single-dose, two-way, crossover *in-vivo*
   Strength: 75 mg
   Subjects: Healthy males and nonpregnant females, general population.
   Additional Comments:

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2. Type of study: Fed
   Design: Single-dose, two-way, crossover *in-vivo*
   Strength: 75 mg
   Subjects: Healthy males and nonpregnant females, general population.
   Additional comments:

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3. Type of study: Fasting
   Design: Single-dose, two-way, crossover *in-vivo*
   Strength: 50 mg
   Subjects: Healthy males and nonpregnant females, general population.
   Additional comments:

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4. Type of study: Fasting
   Design: Single-dose, two-way, crossover *in-vivo*
   Strength: 25 mg
   Subjects: Healthy males and nonpregnant females, general population.
   Additional comments:

Analytes to measure: Diclofenac in plasma

Bioequivalence based on (90% CI): Diclofenac

Waiver request of in-vivo testing: Not Applicable

Please note that Diclofenac Sodium Delayed-Release Tablets, 25 mg, 50 mg, and 75 mg, are the subject of two separate reference products. Two separate applications must be submitted comparing to the appropriate reference products. It may not be necessary to conduct a fed bioequivalence study on the 50-mg strength provided that the fed bioequivalence study on the 75-mg strength is acceptable. Please refer to the Guidance for Industry, *Variations in Drug Products That May be Included in a Single ANDA*, located at http://www.fda.gov/cder/guidance.

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.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.

For modified release products, dissolution profiles generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5 and 6.8 buffer, water) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. The following sampling times are recommended: 1, 2, and 4 hours and every 2 hours thereafter, until at least 80% of the drug is dissolved. Comparative dissolution profiles should include individual tablet data as well as the mean, range, and standard deviation at each time point for twelve tablets. Specifications will be determined upon review of the data submitted in the application.