Contains Nonbinding Recommendations

Draft Guidance on Cefaclor

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Extended-release tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: Eq 500 mg Base
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: None

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2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: Eq 500 mg Base
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: None

Analyte to measure (in appropriate biological fluid): Cefaclor in plasma

Bioequivalence based on (90% CI): Cefaclor

Additional strength: Bioequivalence of 375 mg (Eq Base)to the corresponding reference product strength may be demonstrated based on principles laid out in the FDA guidance on "Bioequivalence Studies with Pharmacokinetic Endpoints for Drugs Submitted Under an ANDA".

Dissolution test method and sampling times:
For modified-release drug products, FDA recommends that applicants develop specific discriminating dissolution methods. Applicants may also use the dissolution method set forth in any related official United States Pharmacopeia (USP) drug product monograph, or in the FDA's database (available at http://www.accessdata.fda.gov/scripts/cder/dissolution/), provided adequate dissolution data supporting the discriminating ability of such a method. If a new dissolution method is developed for the modified-release drug product, FDA recommends that the submission includes the dissolution method development and validation report with the complete information/data supporting the proposed method. 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 abbreviated new drug application.

In addition to the method above, for modified release products, dissolution profiles on 12 dosage units each of test and reference products 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) 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. Include early sampling times of 0.5, 1, 2, and 4 hours and continue every 2 hours until at least 80% of the drug is released, to provide assurance against premature release of drug (dose dumping) from the formulation.