Contains Nonbinding Recommendations

Draft Guidance on Capecitabine

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two way crossover *in-vivo*
   Strength: 500 mg
   Subjects: The study should be conducted either (1) in cancer patients undergoing treatment with Xeloda®; or (2) in former cancer patients who are in remission. Cancer patients should receive individualized regimens that use multiples of the 500-mg strength. If you choose to use former cancer patients who are in remission for the BE studies, then each former patient should receive a single dose of 500 mg.
   Additional comments: The studies may be conducted in the same group of patients or separate groups may be employed for each study. If cancer patients undergoing capecitabine treatment are used, we recommend that the BE study dosing and blood sampling be conducted on the first day of a treatment cycle.

   Submission of an Investigational New Drug Application (IND) is required prior to the conduct of a bioequivalence study for a cytotoxic drug product such as capecitabine (See 21 C.F.R § 320.31).

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2. Type of Study: Fed
   Design: Single-dose, two way crossover *in-vivo*
   Strength: 500 mg
   Subjects: Please see comment above.
   Additional Comments: Please see comment above.

Analytes to measure (in appropriate biological fluid): Capecitabine and its metabolite, 5'-DFCR

Bioequivalence based on (90% CI): Capecitabine

Waiver request of in-vivo testing: 150 mg based on (i) acceptable bioequivalence studies on the 500 mg strengths, (ii) proportionally similar 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.