Contains Nonbinding Recommendations

Draft Guidance on Carbamazepine

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Extended Release Capsules/Oral

Recommended studies: 3 studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover *in-vivo*
   Strength: 300 mg
   Subjects: Normal healthy males and females, general population.
   Additional Comments: Female subjects should not be enrolled in bioequivalence studies of carbamazepine, if they are pregnant. Only females who are either surgically sterile or practicing a recognized safe method of contraception should be included in a study. You should clearly define in the study protocol what is considered a "safe method of contraception".

   Bioequivalence studies conducted for this product, may be referenced to support a request for a waiver of evidence of *in vivo* bioequivalence for generic products referencing EQUETRO. Please submit separate applications for each RLD.

---

2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover *in-vivo*
   Strength: 300 mg
   Subjects: Normal healthy males and females, general population.
   Additional comments: Please see above comment

---

3. Type of study: Fasting (capsule compared to RLD, sprinkled on a spoonful of applesauce)
   Design: Single-dose, two-treatment, two-period crossover *in-vivo*
   Strength: 300 mg
   Subjects: Normal healthy males and females, general population.
   Additional Comments: Please see above comment

Analytes to measure (in appropriate biological fluid): Carbamazepine in plasma

Bioequivalence based on (90% CI): Carbamazepine

Recommended Mar 2004; November 2007

Waiver request of in-vivo testing: 100 mg and 200 mg based on (i) acceptable bioequivalence studies on the 300 mg strength, (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.

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. Please include early sampling times of 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. Specifications will be determined upon review of the data submitted in the application.