Contains Nonbinding Recommendations

Guidance on Phenytoin Sodium

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: Phenytoin Sodium

Form/Route: Extended Capsule/Oral

Recommended studies: 4 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: Single-dose of 300 mg (3 X 100 mg)
   Subjects: Normal healthy males and females, general population.
   Additional Comments: Washout period of at least 14 days. The single dose studies for fasting and fed can be conducted as single dose, two- treatment, four periods, replicated design. The strength(s) designated in the Orange Book as the RLD should be used in the studies.

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2. Type of study: Fed
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: Single-dose of 300 mg (3 X 100 mg)
   Subjects: Normal healthy males and females, general population.
   Additional comments: Please see comments above.

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3. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: Single-dose of 300 mg (10 X 30 mg)
   Subjects: Normal healthy males and females, general population.
   Additional Comments: Please see comments above.

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4. Type of study: Fed
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: Single-dose of 300 mg (10 X 30 mg)
   Subjects: Normal healthy males and females, general population.
   Additional comments: Please see comments above.

Analytes to measure: Phenytoin in plasma

Bioequivalence based on (90% CI): Phenytoin

Waiver request of in-vivo testing: Not applicable.

Dissolution test method and sampling times:

Please conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products using the USP method.

In addition to the method above, 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.