Contains Nonbinding Recommendations

Draft Guidance on Topiramate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-way, crossover *in-vivo*
   Strength: 25 mg
   Subjects: Normal healthy males and females, general population
   Additional Comments: Females must have a negative baseline pregnancy test within 24 hours prior to receiving the drug. Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study.

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2. Type of study: Fed
   Design: Non-replicate *in-vivo*
   Strength: 25 mg
   Subjects: Normal healthy males and females, general population
   Additional comments: Please see comment above.

Analytes to measure: Topiramate in plasma

You may consider truncation of the AUC at 72 hours ($AUC_{0-72\ hr}$) in lieu of AUCt and AUCi for long half-life drugs with low variability in clearance.

Bioequivalence based on (90% CI): Topiramate

Waiver request of in-vivo testing: 50 mg, 100 mg and 200 mg based on (i) acceptable bioequivalence studies on the 25 mg strength, (ii) acceptable dissolution testing across all strengths, and (iii) proportional similarity in the formulations across 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.