

Draft Guidance on Topiramate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Recommended studies: 2 studies

1. Type of study: Fasting

Design: Single-dose, two-way crossover in vivo

Strength: 100 mg

Subjects: Healthy males, general population.

Additional comments: Due to the risk of teratogenicity of topiramate, the study should be conducted in healthy male volunteers.

2. Type of study: Fed

Design: Single-dose, two-way crossover in vivo

Strength: 100 mg

Subjects: Healthy males, general population.

Additional comments: Please see comment above. Please refer to the Amantadine Hydrochloride Tablet Draft Guidance for additional information regarding fed studies.

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

You may consider truncation of the AUC at 72 hours (AUC₀₋₇₂) in lieu of AUC_t and AUC_i for long half-life drugs with low variability in clearance.

Bioequivalence based on (90% CI): Topiramate

Waiver request of in vivo testing: 25 mg, 50 mg and 200 mg based on (i) acceptable bioequivalence studies on the 100 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths. Please refer to the Mirtazapine Tablet Draft Guidance for additional information regarding waivers of in vivo testing.

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.accessdata.fda.gov/scripts/cder/dissolution/>. 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.