

Contains Nonbinding Recommendations
Draft Guidance on Felbamate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Tablets/Oral

Recommended studies: 1 study

Type of study: Fasting

Design: Multiple-dose, two-way, steady-state crossover in-vivo

Strength: 600 mg

Subjects: Male and non-pregnant female epilepsy patients already established on felbamate monotherapy or adjunctive therapy. The patients to be enrolled in the study should already be on a stable mono- or adjunct therapy regimens and these regimens should not change for the duration of the study.

Additional Comments:

1. Steady-state felbamate plasma concentrations can be confirmed by obtaining at least three consecutive measurements of plasma felbamate concentrations prior to dosing. Concentrations should be obtained at the same time each day.
2. Patients who receive multiples of 600 mg tablets of felbamate per day (1800-3600 mg/day in three divided doses) would be eligible for the study by continuing their established maintenance dose. Dose should be included in the Analysis of Variance (ANOVA) statistical model. Dose normalization is not advised.
3. No washout period is necessary between treatment periods.
4. Sponsors may submit a protocol for review and comment prior to conducting the study.

Please also consider the following additional safety monitoring:

- a. If any evidence of bone marrow (hematologic) depression occurs, felbamate treatment should be discontinued and a hematologist consulted to ensure appropriate medical care.
- b. Additional criteria for exclusion from the study relative to baseline:
 - i. two-fold increase in the highest, 2-day pre-study seizure frequency,
 - ii. single generalized, tonic-clonic seizure if none occurred during pre-treatment screening, and/or,
 - iii. significant prolongation of generalized, tonic-clonic seizures.

Analytes to measure: Felbamate in plasma

Bioequivalence based on (90% CI): Felbamate

Waiver request of in-vivo testing: 400 mg based on (i) acceptable bioequivalence studies on the 600 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of 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.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.