

Draft Guidance on Felbamate

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

Active Ingredient: Felbamate

Dosage Form; Route: Tablet; oral

Recommended Study: One study

Study 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.

Also consider the following additional safety monitoring:

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

Analyte to measure (in appropriate biological fluid): 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: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods web site, available to the public at the following location: <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. 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 abbreviated new drug application (ANDA).