

Draft Guidance on Vigabatrin

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Dosage Form; Route: Tablet; oral

Recommended Studies: A multiple-dose, two-treatment, two-way, steady-state crossover in vivo pharmacokinetic bioequivalence study in adult refractory complex partial-seizure patients.

1. Type of study: A multiple-dose, two-treatment, two-way, steady-state pharmacokinetic bioequivalence (BE) study
Design: Two-way crossover in vivo
Strength: 500 mg
Subjects: Adult refractory complex partial-seizure adult patients who are already on established vigabatrin adjunctive therapy

Additional comments:

1. The study drug should not be given with other drugs associated with serious adverse ophthalmic effects, such as retinopathy.
2. Females should not be pregnant or lactating, and, if applicable, should practice abstinence or contraception during the study.
3. The study design (e.g., inclusion/exclusion criteria) and procedures (e.g., safety monitoring) should address all of the elements related to patient safety specified in the reference listed drug (RLD) label. Vigabatrin was approved with a risk evaluation and mitigation strategy (REMS), which restricts its use. All pertinent elements of the REMS must be incorporated into the protocol and informed consent.
4. Patients who are receiving a stable dosage of vigabatrin twice daily would be eligible to participate in the study by continuing their established maintenance dose. FDA recommends that studies not be conducted using healthy subjects.
5. According to the randomization schedule, an equal number of patients should receive either the generic formulation (Treatment A) or the reference formulation (Treatment B) in the same dose as administered prior to the study every 12 hours until the steady state is achieved. Patients are then switched to the other product for a second period of the same duration. No washout period is necessary between the two treatment periods. After the study is completed, patients can continue on their current dose of vigabatrin using an approved vigabatrin product, as prescribed by their clinicians.
6. Attainment of steady state should be confirmed with at least three consecutive trough levels.

7. Blood sampling for BE should consist of appropriate sampling times over a 12-hour period following attainment of steady state.
 8. Investigators should refer to the Warnings, Precautions, Contraindications, and Adverse Reactions in the FDA-approved labeling and follow the directions closely.
-

Analytes to measure: Vigabatrin in plasma

Bioequivalence based on (90% CI): Vigabatrin

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods website 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).