

Contains Nonbinding Recommendations

Draft Guidance on Rifaximin

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Tablet/Oral

Recommended studies: 3 studies

1. Type of study: Fasting Bioequivalence (BE) Study with Pharmacokinetic (PK) endpoints
Design: Single-dose, two-way crossover in-vivo
Strength: 550 mg
Subjects: Healthy males and nonpregnant females, general population.
Additional Comments: Applicants may consider using a reference-scaled average bioequivalence approach for rifaximin. If using this approach, please provide evidence of high variability in the bioequivalence parameters of AUC and/or C_{max} (i.e., within-subject variability $\geq 30\%$). Please refer to the Progesterone Capsule Draft Guidance for additional information regarding highly variable drugs.

2. Type of study: Fed BE Study with Pharmacokinetic (PK) endpoints
Design: Single-dose, two-way crossover in-vivo
Strength: 550 mg
Subjects: Healthy males and nonpregnant females, general population.
Additional Comments: Please also see additional comment above.

3. Type of study: BE Study with Clinical Endpoint
Design: Randomized, double blind, parallel, placebo controlled in vivo
Strength: 200 mg (dose: three times daily for 3 days)
Subjects: Male and nonpregnant female subjects with traveler's diarrhea
Additional Comments:
 - (1) For details on the design of BE study with clinical endpoint please refer to the Rifaximin Draft Guidance, 200-mg strength.
 - (2) The formulation of the 550-mg strength should be proportionally similar to that of the 200 mg strength.

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

Bioequivalence based on (90% CI): Rifaximin

Waiver request of *in-vivo* testing: Not applicable

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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.