

**Draft Guidance on Fidaxomicin**

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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:** Fidaxomicin

**Dosage Form; Route:** Tablet; oral

**Recommended Studies:** Two options

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**Option 1:**

If the test product formulations are qualitatively and quantitatively (Q1/Q2) the same as the Reference Listed Drug (RLD) with respect to inactive ingredients, bioequivalence (BE) may be established by conducting both an in vitro, comparative dissolution study and an in vivo, BE study with pharmacokinetic (PK) endpoints.

In vitro dissolution study:

Comparative dissolution data should be provided for 12 tablets each of test and reference products, in each of the multiple media covering physiologically relevant pH range. It is acceptable to add a small amount of surfactant, if necessary. The selection of dissolution apparatus, agitation speed, sampling time, and surfactant level should be justified. An f2 test should be performed using mean profiles to ensure comparable test (T) and reference (R) product drug release under a range of pH conditions. The f2 test comparing T vs. R in each medium should be between 50 and 100.

In vivo BE study with PK endpoint:

1. Type of study: Fasting  
Design: Single-dose, two-way crossover, in vivo  
Strength: 200mg (Dose: 1x200 mg)  
Subjects: Healthy male and non-pregnant female adults, general population  
Additional Comments: None
  
2. Type of study: Fed  
Design: Single-dose, two-way crossover, in vivo  
Strength: 200mg (Dose: 1x200 mg)  
Subjects: Healthy male and non-pregnant female adults, general population  
Additional Comments: None

**Analytes to measure (in appropriate biological fluid):** Fidaxomicin and its active metabolite, OP-1118 in plasma

Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and Cmax.

**Bioequivalence based on (90% CI):** Fidaxomicin

**Waiver request of in vivo testing:** Not Applicable

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**Option 2:**

If the test product formulations are not Q1/Q2 the same as the RLD with respect to inactive ingredients, BE should be established by conducting an in vivo study with clinical endpoints in patients with Clostridium difficile Associated Diarrhea (CDAD). We recommend that any sponsor choosing this option submit its protocol to the OGD Division of Clinical Review for review and concurrence prior to initiating the study.

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**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/>. 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 abbreviated new drug application (ANDA).