

Draft Guidance on Bedaquiline Fumarate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Tablet; Oral

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover, in vivo
Strength: 100mg (Dose: 100 mg)
Subjects: Healthy males and non-pregnant females, general population
Additional Comments: Due to QT prolongation associated with SIRTURO, electrocardiography (ECGs) should be closely monitored.

2. Type of study: Fed
Design: Single-dose, two-way crossover, in vivo
Strength: 100 mg (Dose: 100 mg)
Subjects: Healthy males and non-pregnant females, general population
Additional Comments: See additional comments above.

Analytes to measure: Bedaquiline in plasma

Bioequivalence based on (90% CI): Bedaquiline

Waiver request of in vivo testing: Not Applicable

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.

Information Regarding Long Half-Life Drugs

For an oral immediate release product with a long elimination half-life drug (>24 hrs), applicants can conduct a single-dose, crossover study, provided an adequate washout period is used. If the crossover study is problematic, BE applicants can use a BE study with a parallel design. For

either a crossover or parallel study, sample collection time should be adequate to ensure completion of gastrointestinal transit of the drug product and absorption of the drug substance (which usually occurs within approximately 2 to 3 days). **C_{max}** and a suitable truncated AUC can be used to characterize peak and total drug exposure, respectively. For drugs that demonstrate low intra-subject variability in distribution and clearance, an AUC truncated at 72 hour (**AUC_{0-72hr}**) can be used in place of **AUC_{0-t}** or **AUC_{0-inf}**. For drugs demonstrating high intra-subject variability in distribution and/or clearance, AUC truncation should not be used.