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Draft Guidance on Atovaquone

October 2024

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredient: Atovaquone

Dosage Form: Tablet

Route: Oral

Strength: 250 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 250 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of atovaquone. Alternatively, a parallel study design may be considered.

Analyte to measure: Atovaquone in plasma

Bioequivalence based on (90% CI): Atovaquone

Waiver request of in vivo testing: Not applicable

Dissolution test method and sampling times: The dissolution information for this drug product can be found in the FDA's Dissolution Methods database, http://www.accessdata.fda.gov/scripts/cder/dissolution. Conduct comparative dissolution testing on 12 dosage units for each of the test product and reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

Atovaquone is known to be practically insoluble in both water and 0.1 M HCl (<0.0002 mg/mL at 25ºC). Use of conventional aqueous dissolution media with and without surfactant has been found unsuccessful and not reproducible in some laboratories working with atovaquone tablet products. If encountering the same difficulty, consider developing a dissolution method similar to the method available in the Dissolution Database. Although the use of the high alcoholic medium is not considered conventional, it has been found justifiable by the FDA for this drug substance.

Applicants may develop an alternate dissolution testing method for the drug product and submit the dissolution testing results when the application is submitted.

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[1] If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions.*