

Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Fluconazole

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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:	Fluconazole
Dosage Form:	Tablet
Route:	Oral
Strengths:	50 mg, 100 mg, 150 mg, 200 mg
Recommended Studies:	Two options: (1) Biopharmaceutics Classification System (BCS)-based biowaiver or (2) one in vivo bioequivalence study with pharmacokinetic endpoints

I. Option 1: BCS Class I-based biowaiver

A waiver request of in vivo testing for all the strengths of this product may be considered provided that the appropriate documentation regarding high solubility, high permeability and rapid dissolution of the test product and reference listed drug (RLD) as detailed in the most recent version of the FDA guidance for industry on *M9 Biopharmaceutics Classification System-Based Biowaivers*^a is submitted in the application. Applicants may use the information contained in the approved labeling of the RLD. Peer reviewed articles may not contain the necessary details of the testing for the Agency to make a judgment regarding the quality of the studies. A decision regarding the acceptability of the waiver request can only be made upon assessment of the data submitted in the application.

II. Option 2: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 200 mg
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: None

Analyte to measure: Fluconazole in plasma

Bioequivalence based on (90% CI): Fluconazole

Waiver request of in vivo testing: 50 mg, 100 mg, and 150 mg strengths based on (i) acceptable bioequivalence study on the 200 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths

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 all strengths of the test product and RLD.¹ Specifications will be determined upon review of the abbreviated new drug application.

Document History: Recommended May 2007; Finalized May 2008; Revised February 2018, October 2024

Unique Agency Identifier: PSG_019949

^a For the most recent version of a guidance, check the FDA guidance website at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>.

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*.