Fluconazole Tablets

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Expert Committee	Chemical Medicines Monographs 1
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 1 Expert Committee has revised the Fluconazole Tablets monograph. The purpose for the revision is to add *Dissolution Test 3* to accommodate FDA-approved drug products with different dissolution conditions and/or tolerances than the existing dissolution tests.

- *Dissolution Test 3* was validated using a Hypersil BDS C18 brand of L1 column. The typical retention time for fluconazole is about 5.3 min.

The Fluconazole Tablets Revision Bulletin supersedes the currently official Fluconazole Tablets monograph.

Should you have any questions, please contact Shankari Shivaprasad, Senior Scientific Liaison (301-230-7426 or sns@usp.org).

Fluconazole Tablets

DEFINITION

Fluconazole Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of fluconazole ($C_{13}H_{12}F_2N_6O$).

IDENTIFICATION

- The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **PROCEDURE**

Buffer: 0.01 M anhydrous sodium acetate solution. Adjust with glacial acetic acid to a pH of 5.0.

Mobile phase: Methanol, acetonitrile, and *Buffer* (20:10:70)

Standard stock solution: 1.0 mg/mL of USP Fluconazole RS dissolved in water, and diluted with *Mobile phase* to volume. Sonicate the solution, if necessary. [NOTE—The target ratio is about 5% water to 95% *Mobile phase*.]

Standard solution: 0.2 mg/mL of USP Fluconazole RS in *Mobile phase* prepared from the *Standard stock solution*

Sample solution: Weigh NLT 5 Tablets, and disperse in a suitable quantity of water. Sonicate the solution, if necessary. Add a sufficient quantity of *Mobile phase,* sonicate for 5 min, and shake for 30 min. Dilute with *Mobile phase* to volume to obtain a concentration between about 1 and 4 mg/mL, and mix. [NOTE—The target ratio is about 5% water to 95% *Mobile phase*.] Centrifuge a suitable portion of the mixture. Filter and quantitatively dilute a portion of the supernatant with *Mobile phase* to obtain a solution of about 0.2 mg/mL of fluconazole.

Chromatographic system

(See *Chromatography* ⟨621⟩*, System Suitability*.)

Mode: LC

Detector: UV 261 nm

Column: 3.9-mm × 150-mm; 4-µm packing L1

Flow rate: 1 mL/min

Injection size: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 1100 theoretical plates

Tailing factor: NMT 3.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fluconazole ($C_{13}H_{12}F_2N_6O$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Fluconazole RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of fluconazole in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **DISSOLUTION** ⟨711⟩

Test 1

Medium: Water; 500 mL (900 mL for Tablets labeled to contain more than 100 mg)

Apparatus 2: 50 rpm

Time: 45 min

Buffer, Mobile phase, and **System suitability:** Proceed as directed in the *Assay*.

Standard solution: 2 mg/mL of USP Fluconazole RS in *Medium*. Sonicate the solution to facilitate dissolution, if necessary. Quantitatively dilute a portion of this solution with *Medium* to obtain a final concentration similar to the one expected in the *Sample solution*.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system and **System suitability:** Proceed as directed in the *Assay*, making any necessary modifications.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fluconazole ($C_{13}H_{12}F_2N_6O$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Fluconazole RS in the *Standard solution* (mg/mL)
L = label claim (mg/Tablet)
V = volume of *Medium*, 500 or 900 mL

Tolerances: NLT 75% (*Q*) of the labeled amount of $C_{13}H_{12}F_2N_6O$ is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets *Dissolution Test 2*.

Medium: Water; 900 mL (for all Tablet strengths)

Apparatus 2: 50 rpm

Time: 45 min

Mobile phase: Water and acetonitrile (4:1)

Standard stock solution: 1.1 mg/mL of USP Fluconazole RS in methanol

Standard solution: Dilute the *Standard stock solution* with *Medium* to obtain a final concentration of (*L*/900) mg/mL, where *L* is the Tablet label claim in mg.

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

(See *Chromatography* ⟨621⟩*, System Suitability*.)

Mode: LC

Detector: UV 260 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection size: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 1000 theoretical plates

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Calculate the percentage of the labeled amount of fluconazole ($C_{13}H_{12}F_2N_6O$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of the *Standard solution* (mg/mL)
L = label claim (mg/Tablet)
V = volume of *Medium*, 900 mL

Tolerances: NLT 75% (*Q*) of the labeled amount of fluconazole is dissolved.

▲**Test 3:** If the product complies with this test, the labeling indicates that it meets *Dissolution Test 3*.
Medium: Water; 900 mL
Apparatus 2: 50 rpm
Time: 30 min
Buffer: 3.9 g/L of sodium dihydrogen phosphate in water
Mobile phase: Methanol and *Buffer* (45:55). Adjust the pH of the solution to 7.0 with 0.1 N sodium hydroxide solution.
Standard stock solution: 1.0 mg/mL of USP Fluconazole RS in *Mobile phase*
Standard solution: (*L*/900) mg/mL of USP Fluconazole RS in *Medium* from the *Standard stock solution*, where *L* is the Tablet label claim in milligrams
Sample solution: Pass a portion of the solution under test through a suitable filter.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 260 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Flow rate: 1 mL/min
Injection volume: 50 µL
Run time: At least 2 times the retention time of fluconazole
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 2.0
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of fluconazole ($C_{13}H_{12}F_2N_6O$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times 100$$

r_U = peak response of fluconazole from the *Sample solution*
r_S = peak response of fluconazole from the *Standard solution*
C_S = concentration of USP Fluconazole RS in the *Standard solution* (mg/mL)
L = label claim (mg/Tablet)
V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (*Q*) of the labeled amount of fluconazole is dissolved.▲ (RB 1-Feb-2020)

- **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩
USP Fluconazole RS