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Flucytosine Capsules

DEFINITION
Flucytosine Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of flucytosine ($C_4H_4FN_3O$).

IDENTIFICATION
Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet Absorption*:** 197U
Wavelength range: 260–350 nm
Diluent: 0.1 N hydrochloric acid
Standard solution: 8 µg/mL of USP Flucytosine RS in *Diluent*
Sample stock solution: Nominally 1 mg/mL of flucytosine in *Diluent* prepared as follows. Remove the contents of Capsules (NLT 20) as completely as possible, and weigh. Transfer a portion of the powder, nominally equivalent to 250 mg of flucytosine, to a 250-mL volumetric flask. Add 50 mL of *Diluent*, shake by mechanical means for 30 min and dilute with *Diluent* to volume. Pass the solution through a suitable membrane filter of 0.45-µm pore size.
Sample solution: Nominally 8 µg/mL of flucytosine in *Diluent* from *Sample stock solution*
Blank: *Diluent*
Acceptance criteria: Meet the requirements▲ (USP 1-May-2022)

Change to read:

• **B.** ▲The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2022)

ASSAY
Change to read:

• **Procedure**

▲**Buffer:** 13.6 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 2.0.
Solution A: *Buffer* and methanol (98:2)
Solution B: *Buffer* and methanol (85:15)
Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
5	100	0
10	0	100
35	0	100
35.1	100	0
45	100	0

Diluent: Dissolve 13.6 g of monobasic potassium phosphate in 980 mL of water. Add 20 mL of methanol and mix.
Standard solution: 0.05 mg/mL of USP Flucytosine RS in *Diluent*
Sample solution: Nominally 0.05 mg/mL of flucytosine in *Diluent* prepared as follows. Remove the contents of Capsules (NLT 10) as completely as possible, and weigh. Transfer a portion of the powder, nominally equivalent to 10 mg of flucytosine, to a 200-mL volumetric flask. Add 100 mL of *Diluent* and shake for 30 min. Dilute with *Diluent* to volume and mix. Pass a portion of the solution under test through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 284 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1.1 mL/min

Injection volume: 20 µL

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 flucytosine ($C_4H_4FN_3O$) in the portion of Capsules taken:

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

r_U = peak response of flucytosine from the *Sample solution*

r_S = peak response of flucytosine from the *Standard solution*

C_S = concentration of USP Flucytosine RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of flucytosine in the *Sample solution* (mg/mL)▲ (USP 1-May-2022)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution ⟨711⟩**

Medium: Water; 900 mL

Apparatus 2: 75 rpm

Time: 60 min

▲▲ (USP 1-May-2022)

Standard solution: USP Flucytosine RS in *Medium*

Sample solution: Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.

▲**Instrumental conditions**

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV

Analytical wavelength: 276 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of flucytosine ($C_4H_4FN_3O$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times D \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of USP Flucytosine RS in the *Standard solution* (mg/mL)

D = dilution factor of the *Sample solution*

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)▲ (USP 1-May-2022)

Tolerances: NLT 80% (Q) of the labeled amount of flucytosine ($C_4H_4FN_3O$) is dissolved.

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

Add the following:

▲**IMPURITIES**

• **Organic Impurities**

Buffer, Solution A, Solution B, Mobile phase, and **Diluent:** Prepare as directed in the *Assay*.

Sensitivity solution: 0.00015 mg/mL of USP Flucytosine RS in *Diluent*

Standard solution: 0.00030 mg/mL of USP Flucytosine RS and 0.00045 mg/mL of USP Fluorouracil RS in *Diluent*

Sample solution: Nominally 0.3 mg/mL of flucytosine in *Diluent* prepared as follows. Remove the contents of Capsules (NLT 10) as completely as possible, and weigh. Transfer a portion of the powder, nominally equivalent to 15 mg of flucytosine, to a 50-mL volumetric flask. Add 25 mL of *Diluent* and shake for 30 min. Dilute with *Diluent* to volume and mix. 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: 1.1 mL/min

Injection volume: 20 µL

System suitability

Samples: *Sensitivity solution* and *Standard solution*

Suitability requirements

Relative standard deviation: NMT 5.0% each for flucytosine and fluorouracil, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of fluorouracil in the portion of Capsules taken:

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

r_U = peak response of fluorouracil from the *Sample solution*

r_S = peak response of fluorouracil from the *Standard solution*

C_S = concentration of USP Fluorouracil RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of flucytosine in the *Sample solution* (mg/mL)

Calculate the percentage of any unspecified degradation product in the portion of Capsules taken:

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

r_U = peak response of any unspecified degradation product from the *Sample solution*

r_S = peak response of flucytosine from the *Standard solution*

C_S = concentration of USP Flucytosine RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of flucytosine in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Flucytosine	1.0	—
Fluorouracil	2.0	0.15
Any unspecified degradation product	—	0.10
Total impurities	—	0.3▲ (USP 1-May-2022)

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in tight, light-resistant containers. ▲Store at controlled room temperature.▲ (USP 1-May-2022)

Change to read:

• **USP REFERENCE STANDARDS ⟨11⟩**

USP Flucytosine RS

▲ USP Fluorouracil RS ▲ (USP 1-May-2022)

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
FLUCYTOSINE CAPSULES	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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