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Fluoxetine Oral Solution

DEFINITION

Fluoxetine Oral Solution contains an amount of Fluoxetine Hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of fluoxetine ($C_{17}H_{18}F_3NO$). It may contain one or more preservatives.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197S**▲ (CN 1-May-2020)

Sample solution: Transfer a volume of Oral Solution, equivalent to 20 mg of fluoxetine, to a separatory funnel. Add 5.0 mL of water and 0.5 mL of 1 N sodium hydroxide, extract with 5 mL of chloroform, and discard the aqueous layer. Evaporate the remaining layer to dryness, and dissolve the residue in 0.4 mL of chloroform.

Acceptance criteria: Meets the requirements

ASSAY

• **Procedure**

Buffer: Triethylamine and water (1:98), adjusted with phosphoric acid to a pH of 6.0

Mobile phase: Acetonitrile and *Buffer* (50:50)

Standard solution: 45 µg/mL of USP Fluoxetine Hydrochloride RS in *Mobile phase*

Sample solution: Nominally 40 µg/mL of fluoxetine from Oral Solution in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; packing L10

Flow rate: 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 fluoxetine ($C_{17}H_{18}F_3NO$) in the portion of Oral Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Fluoxetine Hydrochloride RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of fluoxetine in the *Sample solution* (µg/mL)

M_{r1} = molecular weight of fluoxetine, 309.33

M_{r2} = molecular weight of fluoxetine hydrochloride, 345.79

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Deliverable Volume ⟨698⟩**

For multiple-unit containers

Acceptance criteria: Meets the requirements

- **Uniformity of Dosage Units ⟨905⟩**

For single-unit containers

Acceptance criteria: Meets the requirements

IMPURITIES

- **Organic Impurities**

Solution A: 4.3 g/L of sodium 1-octanesulfonate and 13.8 g/L of monobasic sodium phosphate in water adjusted with phosphoric acid to a pH of 3.0

Solution B: Methanol, acetonitrile, and *Solution A* (26:21:53)

Solution C: Methanol, acetonitrile, and *Solution A* (22:35:43)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution B (%)	Solution C (%)
0	100	0
13	100	0
15	0	100
29	0	100
30	100	0
End	100	0

Diluent: Methanol, acetonitrile, and *Solution A* (30:10:60)

Impurity identification solution: Nominally 2.0 mg/mL of USP Fluoxetine Hydrochloride RS prepared as follows. Transfer a suitable quantity of USP Fluoxetine Hydrochloride RS to a container, dissolve in 1 N sulfuric acid, and heat at 85° for 1 h.

System suitability solution: 0.1 mg/mL of USP Fluoxetine Hydrochloride RS prepared as follows. Transfer 10 mg of USP Fluoxetine Hydrochloride RS to a 100-mL volumetric flask. Add 1.0 mL of *Impurity identification solution*. Dissolve in and dilute with *Diluent* to volume.

Sample solution: Nominally 1.9 mg/mL of fluoxetine from Oral Solution in *Diluent*

Dilute sample solution: Nominally 76 µg/mL of fluoxetine from *Sample solution* in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

Suitability requirements: The retention time of any peak, except the fluoxetine peak, is less than 13 min.

Analysis

Samples: *Sample solution* and *Dilute sample solution*

Calculate the percentage of each impurity in the portion of Oral Solution taken:

$$\text{Result} = \{r_i/[r_T + (D \times r_{UD})]\} \times 100$$

r_i = peak response of each impurity from the *Sample solution*

r_T = sum of all the peak responses excluding fluoxetine from the *Sample solution*

D = dilution factor between the *Sample solution* and the *Dilute sample solution*, 25

r_{UD} = peak response of fluoxetine from the *Dilute sample solution*

Acceptance criteria

Any individual impurity: NMT 0.4%

Total impurities: NMT 0.8%

SPECIFIC TESTS

• **pH** ⟨791⟩**:** 2.5–4.5

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

• **USP Reference Standards** ⟨11⟩

USP Fluoxetine Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
FLUOXETINE ORAL SOLUTION	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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