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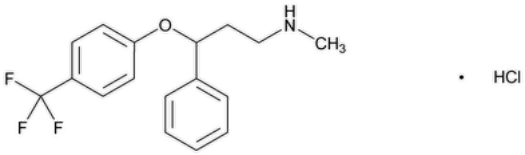
Fluoxetine Hydrochloride



• HCl

$C_{17}H_{18}F_3NO \cdot HCl$ 345.79

Benzenepropanamine, *N*-methyl-γ-[4-(trifluoromethyl)phenoxy]-, hydrochloride, (±);
(±)-*N*-Methyl-3-phenyl-3-[(α,α,α-trifluoro-*p*-tolyl)oxy]propylamine, hydrochloride;
N-Methyl-3-phenyl-3-[4-(trifluoromethyl)phenoxy]propan-1-amine hydrochloride CAS RN®: 56296-78-7; UNII: I9W7N6B1KJ.

DEFINITION

Fluoxetine Hydrochloride contains NLT 98.0% and NMT 102.0% of fluoxetine hydrochloride ($C_{17}H_{18}F_3NO \cdot HCl$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

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

• **B.** **Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride*:** Meets the requirements

Add the following:

▲• **C.** 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-Dec-2019)

ASSAY

Change to read:

• **Procedure**

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

Mobile phase: Stabilizer-free tetrahydrofuran, methanol, and *Buffer* (30:10:60)

Standard solution: 0.11 mg/mL of USP Fluoxetine Hydrochloride RS in *Mobile phase*

Sample solution: 0.11 mg/mL of Fluoxetine Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 227 nm

Column: 4.6-mm × 25-cm; 5-µm base-deactivated packing L7

Flow rate: 1 mL/min

Injection volume: 10 µL

▲**Run time:** NLT 1.2 times the retention time of fluoxetine▲ (USP 1-Dec-2019)

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT ▲0.73%▲ (USP 1-Dec-2019)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of fluoxetine hydrochloride ($C_{17}H_{18}F_3NO \cdot HCl$) in the portion of Fluoxetine Hydrochloride 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 Fluoxetine Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = concentration of Fluoxetine Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

Change to read:

• **Organic Impurities**

Buffer and **Mobile phase:** Prepare as directed in the *Assay*.

System suitability solution: Dissolve about 22 mg of USP Fluoxetine Hydrochloride RS in 10 mL of 1 N sulfuric acid ▲VS .▲ (USP 1-Dec-2019) Heat at 85° for 3 h. Cool, and transfer 0.4 mL of this solution to a 25-mL volumetric flask. Add 28 mg of USP Fluoxetine Hydrochloride RS, 1 mg of USP Fluoxetine Related Compound A RS, and 1 mg of USP Fluoxetine Related Compound B RS. Dilute with *Mobile phase* to volume.

▲**Sensitivity solution:** 0.0028 mg/mL of USP Fluoxetine Hydrochloride RS in *Mobile phase*▲ (USP 1-Dec-2019)

Sample solution A: 5.6 mg/mL of Fluoxetine Hydrochloride in *Mobile phase*

Sample solution B: 1.1 mg/mL of Fluoxetine Hydrochloride from *Sample solution A* in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 5-µm base-deactivated packing L7

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 2 times the retention time of fluoxetine

System suitability

Samples: *System suitability solution* ▲and *Sensitivity solution*▲ (USP 1-Dec-2019)

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NMT 1.1 for the ratio of the height of the fluoxetine related compound A peak to the depth of the valley between the fluoxetine and fluoxetine related compound A peaks (measured from the fluoxetine related compound A peak height), ▲*System suitability solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*▲ *(USP 1-Dec-2019)*

Analysis

Samples: *Sample solution A* and *Sample solution B*

Calculate the percentage of fluoxetine related compound A in the portion of Fluoxetine Hydrochloride taken:

$$\text{Result} = [r_{iB}/(r_{iB} + r_{UB})] \times 100$$

r_{iB} = peak response of fluoxetine related compound A from *Sample solution B*

r_{UB} = peak response of fluoxetine from *Sample solution B*

Calculate the percentage of any other impurity in the portion of Fluoxetine Hydrochloride taken:

$$\text{Result} = \{r_{iA}/[r_{TA} + (D \times r_{UB})]\} \times 100$$

r_{iA} = peak response of any other impurity from *Sample solution A*

r_{TA} = sum of all the peak responses excluding fluoxetine from *Sample solution A*

D = dilution factor between *Sample solution A* and *Sample solution B*, 5

r_{UB} = peak response of fluoxetine from *Sample solution B*

Acceptance criteria: See *Table 1*. ▲The reporting threshold is 0.05%.▲ (USP 1-Dec-2019)

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Aminomethyl-1-phenylpropanol[a,b]	0.24	0.25
Fluoxetine related compound B	0.27	0.25
Fluoxetine related compound A	0.94	0.15
Fluoxetine	1.0	—
4-Trifluoromethylphenol	2.17	▲0.10▲ (USP 1-Dec-2019)
Any individual unspecified impurity	—	▲0.10▲ (USP 1-Dec-2019)
Total impurities	—	0.5

[a] 3-Methylamino-1-phenylpropan-1-ol; also known as α-[2-(methylamino)ethyl]benzenemethanol.

[b] This impurity may not be present.

SPECIFIC TESTS

• **Water Determination** ⟨921⟩, *Method I*: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

• **USP Reference Standards** ⟨11⟩

USP Fluoxetine Hydrochloride RS

USP Fluoxetine Related Compound A RS

N-Methyl-3-phenyl-3-[3-(trifluoromethyl)phenoxy]propan-1-amine hydrochloride;
Also known as *N*-Methyl-3-phenyl-3-[(α,α,α-(trifluoro-*m*-tolyl)oxy]propylamine hydrochloride.

$C_{17}H_{18}F_3NO \cdot HCl$ 345.79

USP Fluoxetine Related Compound B RS

N-Methyl-3-phenylpropan-1-amine;
Also known as *N*-Methyl-3-phenylpropylamine.

$C_{10}H_{15}N$ 149.24

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

Topic/Question	Contact	Expert Committee
FLUOXETINE HYDROCHLORIDE	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

Most Recently Appeared In:
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