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Fluvoxamine Maleate Tablets

DEFINITION

Fluvoxamine Maleate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of fluvoxamine maleate ($C_{15}H_{21}F_3N_2O_2 \cdot C_4H_4O_4$).

IDENTIFICATION

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

ASSAY

Change to read:

- **Procedure**

Solution A: 8 g/L of 1-pentanesulfonic acid sodium salt and ▲1.1▲ (ERR 1-May-2023) g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 3.00 ± 0.05.

Mobile phase: Acetonitrile and *Solution A* (38:62)

System suitability solution: Transfer 6 mg of fluvoxamine maleate to a 50-mL volumetric flask. Heat the sample at 120° for 10 min. Cool to room temperature, and add 3.0 mL of 0.1 N hydrochloric acid. Heat the solution in a water bath for 10 min. Cool to room temperature, add 50 mg of fluvoxamine maleate, and dissolve in 25 mL of *Mobile phase*. Dilute with *Mobile phase* to volume.

Standard solution: 0.05 mg/mL of USP Fluvoxamine Maleate RS in *Mobile phase*

Sample stock solution: Nominally 1 mg/mL of fluvoxamine maleate from Tablets prepared as follows. Finely powder NLT 20 Tablets and transfer a portion of the powder to a suitable volumetric flask. Add 50% of the flask volume of *Mobile phase*. Sonicate for 15 min followed by mechanical shaking for 15 min. Dilute with *Mobile phase* to volume. Centrifuge a portion of this solution for 10 min.

Sample solution: Nominally 0.05 mg/mL from *Sample stock solution* diluted with *Mobile phase*. Pass through a filter of 0.45-µm or finer pore size.

Chromatographic system

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

Mode: LC

Detector: UV 234 nm. For *Identification B*, use a diode array detector in the range of 210–400 nm.

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

Column temperature: 40°

Flow rate: 1.7 mL/min

Injection volume: 20 µL

Run time: NLT 2.5 times the retention time of fluvoxamine

System suitability

Samples: *System suitability solution* and *Standard solution*

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

Suitability requirements

Resolution: NLT 2.0 between *Z*-isomer and fluvoxamine maleate; NLT 5.0 between succinyl fluvoxamine and the *Z*-isomer, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fluvoxamine maleate ($C_{15}H_{21}F_3N_2O_2 \cdot C_4H_4O_4$) in the portion of Tablets taken:

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

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Medium: Water; 900 mL, degassed

Apparatus 2: 50 rpm

Time: 30 min

Standard solution: USP Fluvoxamine Maleate RS in *Medium*

Sample solution: Centrifuge a portion of the solution under test, and dilute with *Medium*, if necessary. [Note—The use of a centrifuge speed of NLT 2000 rpm for NLT 10 min may be suitable.]

Instrumental conditions

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

Mode: UV

Analytical wavelength: 246 nm

Analysis

Samples: *Standard solution* and *Sample solution*

When there are known interferences due to excipients, excipient interference corrections may be applied, as necessary.

Calculate the percentage of the labeled amount of fluvoxamine maleate ($C_{15}H_{21}F_3N_2O_2 \cdot C_4H_4O_4$) 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 the *Standard solution* (mg/mL)

D = dilution factor for the *Sample solution*, if needed

V = volume of *Medium,* 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of fluvoxamine maleate ($C_{15}H_{21}F_3N_2O_2 \cdot C_4H_4O_4$) is dissolved.

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

IMPURITIES

• **Organic Impurities, Procedure 1**

Use *Procedure 1* when the impurity profile includes aminoethyl desmethoxy fluvoxamine, dealkyl benzyl fluvoxamine, or fluvoxamine maleamide.

Solution A, Mobile phase, System suitability solution, Standard solution, and **System suitability:** Proceed as directed in the *Assay.*

Sample solution: Use the *Sample stock solution,* prepared as directed in the *Assay*.

Chromatographic system: Proceed as directed in the *Assay*, except for the *Run time.*

Run time: NLT 6 times the retention of fluvoxamine

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each degradation product in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak area of each degradation product from the *Sample solution*

r_S = peak area of fluvoxamine from the *Standard solution*

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

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

F = relative response factor for each degradation product (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Maleic acid[a]	0.19	—	—
Succinyl fluvoxamine[b]	0.50	1.0	0.8
Aminoethyl fluvoxamine[c]	0.67	0.71	0.2
Z-isomer[d]	0.79	1.0	0.5
Fluvoxamine	1.0	—	—
Aminoethyl desmethoxy fluvoxamine[e]	1.18	1.0	0.2
Dealkyl benzyl fluvoxamine[f]	1.74	1.0	0.2
Desmethoxy fluvoxamine[g]	2.00	1.0	0.2
Fluvoxamine oxime[h]	3.45	1.66	0.2
Valerophenone analog[i]	4.2	3.3	0.2
Fluvoxamine maleamide[j]	4.3	1.0	0.2
Any individual unspecified degradation product	—	1.0	0.1
Total degradation products	—	—	1.8

[a] This is the counterion. It is not to be reported or included in the total degradation products for the drug product.

[b] 5-Methoxy-1-[4-(trifluoromethyl)phenyl]-1-pentanone (*E*)-*O*-[2-[(2-succinyl)amino]ethyl]oxime.

[c] (*E*)-5-Methoxy-1-[4-(trifluoromethyl)phenyl]pentan-1-one-*O*-{2-[(2-aminoethyl)amino]ethyl} oxime.

[d] (*Z*)-5-Methoxy-1-[4-(trifluoromethyl)phenyl]pentan-1-one *O*-(2-aminoethyl) oxime.

[e] (*E*)-1-[4-(Trifluoromethyl)phenyl]pentan-1-one *O*-{2-[(2-aminoethyl)amino]ethyl} oxime.

[f] (*E*)-2-Phenyl-1-[4-(trifluoromethyl)phenyl]ethan-1-one *O*-(2-aminoethyl) oxime.

[g] (*E*)-1-[4-(Trifluoromethyl)phenyl]pentan-1-one *O*-(2-aminoethyl) oxime.

[h] (*E*)-5-Methoxy-1-[4-(trifluoromethyl)phenyl]pentan-1-one oxime.

[i] 5-Methoxy-1-(4-(trifluoromethyl)phenyl)pentan-1-one.

[j] (2*Z*,9*E*)-4-Oxo-10-[4-(trifluoromethyl)phenyl]-8,15-dioxa-5,9-diazahexadeca-2,9-dienoic acid.

• **Organic Impurities, Procedure 2**

Use *Organic Impurities, Procedure 2* when the impurity profile includes desfluoro fluvoxamine.

Solution A: 13.6 g/L of sodium acetate in water

Mobile phase: Acetonitrile, methanol, and *Solution A* (30:15:55). To each L add 2 mL of triethylamine, and adjust with glacial acetic acid to a pH of 4.5.

Diluent: Methanol and water (60:40)

System suitability solution: Prepare as directed in the *Assay*.

Standard solution: 0.001 mg/mL of fluvoxamine maleate in *Diluent* prepared by dilution of the *Standard solution* in the *Assay*

Sample stock solution: Prepare as directed in the *Assay*.

Sample solution: Nominally 0.1 mg/mL of fluvoxamine maleate from *Sample stock solution* in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

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

Column temperature: 40°

Flow rate: 2 mL/min

Injection volumes

System suitability solution: 20 µL

Other solutions: 100 µL

Run time: NLT 2.5 times the retention time of fluvoxamine

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.0 between *Z*-isomer and fluvoxamine, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each degradation product in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak area of each degradation product from the *Sample solution*

r_S = peak area of fluvoxamine from the *Standard solution*

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

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

F = relative response factor for each impurity (see *Table 2*)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Desfluoro fluvoxamine[a]	0.58	1.0	0.2
Succinyl fluvoxamine[b]	0.70	1.0	1.2
Aminoethyl fluvoxamine[c]	0.75	1.0	0.2
Z-isomer[d]	0.85	0.5	0.5
Fluvoxamine	1.0	—	—
Desmethoxy fluvoxamine[e]	1.86	1.0	0.2
Fluvoxamine oxime[f]	1.99	1.0	0.2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Valerophenone analog[g]	2.17	1.0	0.2
Any individual unspecified degradation product	—	1.0	0.2
Total degradation products	—	—	1.5

[a] (*E*)-1-[4-(Difluoromethyl)phenyl]-5-methoxypentan-1-one *O*-(2-aminoethyl) oxime.

[b] 5-Methoxy-1-[4-(trifluoromethyl)phenyl]-1-pentanone (*E*)-*O*-[2-[(2-succinyl)amino]ethyl]oxime.

[c] (*E*)-5-Methoxy-1-[4-(trifluoromethyl)phenyl]pentan-1-one-*O*-{2-[(2-aminoethyl)amino]ethyl} oxime.

[d] (*Z*)-5-Methoxy-1-[4-(trifluoromethyl)phenyl]pentan-1-one *O*-(2-aminoethyl) oxime.

[e] (*E*)-1-[4-(Trifluoromethyl)phenyl]pentan-1-one *O*-(2-aminoethyl) oxime.

[f] (*E*)-5-Methoxy-1-[4-(trifluoromethyl)phenyl]pentan-1-one oxime.

[g] 5-Methoxy-1-(4-(trifluoromethyl)phenyl)pentan-1-one.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:**

Preserve in tight containers. Store at controlled room temperature.

• **Labeling:** The labeling indicates which test for *Organic Impurities* is used only if *Procedure 1* is not used.

• **USP Reference Standards** ⟨11⟩

USP Fluvoxamine Maleate RS

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

Topic/Question	Contact	Expert Committee
FLUVOXAMINE MALEATE TABLETS	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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