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Mirtazapine Orally Disintegrating Tablets

DEFINITION

Mirtazapine Orally Disintegrating Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of mirtazapine ($C_{17}H_{19}N_3$).

IDENTIFICATION

Change to read:

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

Standard solution: Dissolve 30 mg of USP Mirtazapine RS in a separatory funnel containing 30 mL of water, and add 30 mL of *n*-hexane. Shake vigorously for 5 min. Allow the solution to separate into two layers. Filter the *n*-hexane layer through glass wool, and evaporate to dryness.

Sample solution: Transfer a quantity of finely powdered Tablets, equivalent to 30 mg of mirtazapine, to a separatory funnel. Add 30 mL of water and 30 mL of *n*-hexane. Shake vigorously for 5 min. Allow the solution to separate into two layers. Filter the *n*-hexane layer through glass wool, and evaporate to dryness.

• **B.** 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**

Diluent: Acetonitrile and water (50:50)

Diluted phosphoric acid: Water and phosphoric acid (1000:3)

Buffer: Dissolve 1 g of monobasic potassium phosphate and 1.7 g of pentanesulfonic acid sodium salt in 1 L of water. Adjust with *Diluted phosphoric acid* to a pH of 4.7 ± 0.1, and filter.

Mobile phase: Acetonitrile and *Buffer* (25:75)

Standard stock solution: 0.3 mg/mL of USP Mirtazapine RS in *Diluent*

Standard solution: 0.036 mg/mL of USP Mirtazapine RS in *Mobile phase* from the *Standard stock solution*

Sample stock solution: 0.3 mg/mL of mirtazapine in *Diluent* (from NLT 20 Tablets, finely powdered). Sonicate for 15 min with occasional swirling, and shake for 30 min. [Note—Alternatively, dissolve 10 Tablets in a volume of a mixture of acetonitrile and water (90:10) to obtain a 0.3 mg/mL solution of mirtazapine. Shake or stir until the mixture is free from lumps.]

Sample solution: Nominally, 0.036 mg/mL of mirtazapine in *Mobile phase* obtained as follows: transfer 40 mL of the *Sample stock solution* into a centrifuge tube, and centrifuge at 3000 rpm for 10 min. Transfer 6.0 mL of the supernatant into a 50-mL volumetric flask, and dilute with *Mobile phase* to volume. Pass the portion through a polypropylene membrane filter of 0.45-µm pore size. Discard at least the first 5 mL of filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 290 nm

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

Flow rate: 1 mL/min

Injection size: 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 mirtazapine ($C_{17}H_{19}N_3$) 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 Mirtazapine RS (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Disintegration ⟨701⟩:** NMT 60 s

• **Dissolution ⟨711⟩**

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 15 min

Sample solution: Sample per *Dissolution ⟨711⟩*. Pass through a filter of 0.45-µm pore size, and discard the first 5 mL of the filtrate.

Standard solution: 33 µg/mL of USP Mirtazapine RS in *Medium*

Instrumental conditions

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

Mode: UV

Analytical wavelength: 316 nm

Blank: *Medium*

Cell: 0.5 cm

Analysis: Determine the percentage of mirtazapine ($C_{17}H_{19}N_3$) dissolved:

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume, 900 mL

L = label claim of mirtazapine (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of mirtazapine ($C_{17}H_{19}N_3$) is dissolved.

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

IMPURITIES

• **Organic Impurities**

Solution A: Dissolve 7.2 g of tetramethylammonium hydroxide pentahydrate in 4 L of water. Add 1 mL of triethylamine. Adjust with phosphoric acid to a pH of 7.4.

Solution B: Acetonitrile, methanol, and tetrahydrofuran (170:145:85)

Diluent: Acetonitrile and water (50:50)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	61	39
6.0	61	39
10.0	46	54
18.4	46	54
18.5	61	39
22.0	61	39

System suitability solution: 0.3 mg/mL of USP Mirtazapine RS in *Diluent*

Standard solution: 0.015 mg/mL each of USP Mirtazapine RS, USP Mirtazapine Related Compound A RS, USP Mirtazapine Related Compound B RS, USP Mirtazapine Related Compound C RS, and USP Mirtazapine Related Compound D RS in *Diluent*

Sample solution: Nominally, 1.5 mg/mL of mirtazapine in *Diluent* from NLT 5 Tablets

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

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

Column temperature: 40°

Flow rate: 1.2 mL/min

Injection size: 10 µL

System suitability

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

Suitability requirements

Tailing factor: NMT 2.0, *System suitability solution*

Relative standard deviation: NMT 2.0%, *System suitability solution*

Resolution: NLT 4.0 between the mirtazapine and mirtazapine related compound D peaks, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual specified impurity in the portion of Tablets taken:

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

r_U = peak response of each individual specified impurity from the *Sample solution*

r_S = peak response of the corresponding related compound from the *Standard solution*

C_S = concentration of each individual impurity in the *Standard solution* (mg/mL)

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

Calculate the percentage of each individual unspecified impurity in the portion of Tablets taken:

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

r_U = peak response of each individual impurity from the *Sample solution*

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

C_S = concentration of mirtazapine in the *Standard solution* (mg/mL)

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

Acceptance criteria: See *Table 2*. [NOTE—Disregard any peak less than 0.05%.]

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Mirtazapine related compound B	0.23	0.5
Mirtazapine related compound C	0.51	0.5
Mirtazapine related compound A	0.62	0.5
Mirtazapine	1.0	—
Mirtazapine related compound D	1.3	0.5
Any individual unspecified degradation product	—	0.5
Total impurities	—	3.0

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Store at controlled room temperature. Protect from light and moisture.

• **USP Reference Standards** (11)

USP Mirtazapine RS

USP Mirtazapine Related Compound A RS

1,2,3,4,10,14b-Hexahydropyrazino[2,1-*a*]pyrido[2,3-*c*][2]benzazepine.
$C_{16}H_{17}N_3$ 251.33

USP Mirtazapine Related Compound B RS

1,2,3,4,10,14b-Hexahydro-2-methylpyrazino[2,1-*a*]pyrido[2,3-*c*][2]benzazepine 2-oxide monohydrate.
$C_{17}H_{19}N_3O \cdot H_2O$ 299.36

USP Mirtazapine Related Compound C RS

2-Methyl-3,4,10,14b-tetrahydrobenzo[*c*]pyrazino[1,2-*a*]pyrido[3,2-*f*]azepin-1(2*H*)-one.
$C_{17}H_{17}N_3O$ 279.34

USP Mirtazapine Related Compound D RS

2-Methyl-1,2,3,4-tetrahydrobenzo[*c*]pyrazino[1,2-*a*]pyrido[3,2-*f*]azepin-10(14b*H*)-one.
$C_{17}H_{17}N_3O$ 279.34

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

Topic/Question	Contact	Expert Committee
MIRTAZAPINE ORALLY DISINTEGRATING TABLETS	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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