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Olanzapine Orally Disintegrating Tablets

DEFINITION

Olanzapine Orally Disintegrating Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of olanzapine ($C_{17}H_{20}N_4S$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

Standard: Add 25 mg of USP Olanzapine RS to a suitable container containing 10 mL of water. Centrifuge for 5 min, and discard the supernatant. Dry the olanzapine under vacuum for 1 h at 60°.

Sample: Place 1 Tablet in 10 mL of water in a centrifuge tube. Centrifuge for 5 min. Wash the precipitate with 5 mL of water, and centrifuge for 5 min. Discard the water, and repeat the process a third time. Dry the olanzapine under vacuum for 1 h at 60°.

Acceptance criteria: Meet the requirements

• **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**

Solution A: Acetonitrile and water (20:80). Add 2 mL of perchloric acid to each liter of the mixture.

Solution B: Acetonitrile and water (60:40). Add 2 mL of perchloric acid to each liter of the mixture.

Diluent: Acetonitrile and water (35:65)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	87	13
10	87	13
20	0	100
26	0	100
26.1	87	13
36	87	13

System suitability solution: 0.1 mg/mL of USP Olanzapine RS and 10 µg/mL of USP Olanzapine Related Compound C RS in *Diluent*

Standard solution: 0.1 mg/mL of USP Olanzapine RS in *Diluent*

Sample stock solution: 0.5–0.6 mg/mL of olanzapine from Tablets (NLT 10), prepared as follows. Transfer the Tablets to a suitable volumetric flask. Add *Diluent* to fill about 80% of the flask volume. Shake mechanically for 10 min, and dilute with *Diluent* to volume.

Sample solution: Nominally 0.1–0.12 mg/mL of olanzapine from the *Sample stock solution* in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 260 nm

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

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between the olanzapine and olanzapine related compound C peaks, *System suitability solution*

Tailing factor: NMT 2.0 for the olanzapine peak, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of olanzapine ($C_{17}H_{20}N_4S$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Disintegration ⟨701⟩**

Test 1: NMT 10 s for each of 6 units

Test 2: If the product complies with this test, the labeling indicates that the product meets USP *Disintegration Test 2*.

Acceptance criteria: NMT 30 s

Change to read:

• **Dissolution ⟨711⟩**

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 10 min

Standard solution: (*L*/900) mg/mL of USP Olanzapine RS in *Medium*

Sample solution: A portion of the solution under test may be either centrifuged or filtered through a suitable membrane filter of 0.45-µm pore size. Discard the first few milliliters. The filtrate or centrifugate may be suitably diluted.

Determine the amount of olanzapine ($C_{17}H_{20}N_4S$) dissolved by using either the *Spectrometric procedure* or *Chromatographic procedure*.

Spectrometric procedure

Instrumental conditions

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

Mode: UV-Vis

Analytical wavelength: 344 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of olanzapine ($C_{17}H_{20}N_4S$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S^{\blacktriangle} \times D_{\blacktriangle\ (\text{USP 1-Aug-2022})} \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

$\blacktriangle D$ = dilution factor of the *Sample solution*$\blacktriangle$ (USP 1-Aug-2022)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Chromatographic procedure

Buffer: 6.8 g/L of sodium acetate in water. Adjust with glacial acetic acid to a pH of 5.0.

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

Chromatographic system

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

Mode: LC

Detector: UV 250 nm

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

Flow rate: 1 mL/min

Injection volume: 10 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 olanzapine ($C_{17}H_{20}N_4S$) dissolved:

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

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

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

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of olanzapine ($C_{17}H_{20}N_4S$) is dissolved.

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

IMPURITIES

Change to read:

• **Organic Impurities**

▲[Note—A few drops of acetonitrile, not to exceed 5% of the final volume, may be added to the *Standard solution* and *Sample solution* before final dilution to reduce foaming.]

Buffer 1: Dissolve 3.3 mL of phosphoric acid in 1 L of water. Adjust with 50% of sodium hydroxide to a pH of 2.55 ± 0.05.

Buffer 2: Dissolve 8.7 g of sodium dodecyl sulfate in 1 L of *Buffer 1*. Mix for NLT 30 min before use.

Buffer 3: Dissolve 18.6 mg of edetate disodium (EDTA) in 1 L of *Buffer 2*. Mix for NLT 30 min before use.

Solution A: Acetonitrile and *Buffer 2* (48:52)

Solution B: Acetonitrile and *Buffer 2* (70:30)

Diluent: Acetonitrile and *Buffer 3* (40:60)

System suitability solution: 20 µg/mL of USP Olanzapine RS and 2 µg/mL each of USP Olanzapine Related Compound B RS and USP Olanzapine Related Compound C RS in *Diluent*

Standard solution: 2 µg/mL of USP Olanzapine RS in *Diluent*

Sensitivity solution: 0.4 µg/mL of USP Olanzapine RS in *Diluent* from the *Standard solution*

Sample solution: Nominally 400 µg/mL of olanzapine from Tablets prepared as follows. Transfer a known quantity of finely crushed powder from Tablets (NLT 20) to a suitable volumetric flask. Add about 60% of the flask volume of *Diluent*. Mechanically shake for 5 min, and sonicate for about 1 min. Dilute with *Diluent* to volume. Pass through a suitable filter of 0.45 µm-pore size. Discard the first 3 mL of the filtrate. [Note—Use freshly crushed powder for the sample preparation. The *Sample solution* should be injected immediately after preparation. Protect the solution from light at all times.]

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	100	0
10	100	0
20	0	100
25	0	100
27	100	0
35	100	0

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

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

Temperatures

Autosampler: 5°

Column: 35°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 3.0 between olanzapine and olanzapine related compound C, *System suitability solution*

Tailing factor: NMT 1.5 for the olanzapine peak, *System suitability solution*

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

Signal-to-noise ratio: NLT 10, *Sensitivity 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 response of each degradation product from the *Sample solution*

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

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

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

F = relative response factor (see *Table 3*)

Acceptance criteria: See *Table 3*. The reporting threshold is 0.1%.

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Olanzapine open ring analog[a] (if present)	0.18	1.0	0.50

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Olanzapine lactam[b]	0.26	1.0	0.50
Olanzapine related compound B	0.30	2.3	0.50
Olanzapine thiolactam[c]	0.34	1.0	0.50
Olanzapine acetyl open ring analog[d] (if present)	0.37	1.0	0.50
Olanzapine related compound C	0.83	0.76	0.50
Olanzapine	1.0	—	—
Any individual unspecified degradation product	—	1.0	0.20
Total degradation products	—	—	1.5▲ (USP 1-Aug-2022)

[a] (*Z*)-3-(Hydroxymethylene)-4-(4-methylpiperazin-1-yl)-1,3-dihydro-2*H*-benzo[*b*][1,4]diazepine-2-thione.

[b] (*Z*)-4-(4-Methylpiperazin-1-yl)-3-(2-oxopropylidene)-1*H*-benzo[*b*][1,4]diazepin-2(3*H*)-one.

[c] (*Z*)-1-{4-(4-Methylpiperazin-1-yl)-2-thioxo-1*H*-benzo[*b*][1,4]diazepin-3(2*H*)-ylidene}propan-2-one.

[d] (*Z*)-(4-(4-Methylpiperazin-1-yl)-2-thioxo-1,2-dihydro-3*H*-benzo[*b*][1,4]diazepin-3-ylidene)methyl acetate.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.

Change to read:

• **Labeling:** When more than one *Disintegration* test is given, the labeling states the *Disintegration* test used only if *Test 1* is not used. ▲▲ (USP 1-Aug-2022)

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Olanzapine RS

▲ USP Olanzapine Related Compound B RS

2-Methyl-10*H*-thieno-[2,3-*b*][1,5]benzodiazepin-4[5*H*]-one;
Also known as 2-Methyl-5,10-dihydro-4*H*-benzo[*b*]thieno[2,3-e][1,4]diazepin-4-one.

$C_{12}H_{10}N_2OS$ 230.29▲ (USP 1-Aug-2022)

USP Olanzapine Related Compound C RS

2-Methyl-4-(4-methylpiperazin-1-yl)-10*H*-benzo[*b*]thieno[2,3-e][1,4]diazepine 4'-*N*-oxide.

$C_{17}H_{20}N_4OS$ 328.43

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

Topic/Question	Contact	Expert Committee
OLANZAPINE ORALLY DISINTEGRATING TABLETS	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

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