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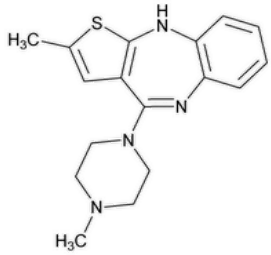
Olanzapine



$C_{17}H_{20}N_4S$ 312.43

10*H*-Thieno[2,3-*b*][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-;

2-Methyl-4-(4-methyl-1-piperazinyl)-10*H*-thieno[2,3-*b*][1,5] benzodiazepine CAS RN®: 132539-06-1; UNII: N7U69T4SZR.

DEFINITION

Olanzapine contains NLT 98.0% and NMT 102.0% of olanzapine ($C_{17}H_{20}N_4S$), calculated on the anhydrous, solvent-free basis.

IDENTIFICATION

Change to read:

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

• **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**

Buffer: Dissolve 6.9 g of monobasic sodium phosphate in 1 L of water. Adjust with phosphoric acid to a pH of 2.5, and dissolve 12 g of sodium dodecyl sulfate in the resulting solution.

Mobile phase: Acetonitrile and *Buffer* (47:53)

System suitability solution: 0.1 mg/mL of USP Olanzapine RS and 0.01 mg/mL of USP Olanzapine Related Compound A RS in *Mobile phase*

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

Sample solution: 0.1 mg/mL of Olanzapine in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 260 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for olanzapine related compound A and olanzapine are 0.8 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between olanzapine related compound A and olanzapine

Tailing factor: 0.8–1.5 for the olanzapine peak

Relative standard deviation: NMT 1.0% for the olanzapine peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of olanzapine ($C_{17}H_{20}N_4S$) in the portion of Olanzapine 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 Olanzapine RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–102.0% on the anhydrous, solvent-free basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Organic Impurities**

Buffer: Dissolve 13 g of sodium dodecyl sulfate in 1500 mL of water. Add 5 mL of phosphoric acid, and adjust with a sodium hydroxide solution to a pH of 2.5.

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

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

Mobile phase: See *Table 1*.

Table 1

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

Edetate disodium solution: 37 mg/L of edetate disodium in *Buffer*

Diluent: Acetonitrile and *Edetate disodium solution* (40:60)

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

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

Sample solution: 0.4 mg/mL of Olanzapine in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

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

Temperatures

Column: 35°

Sample: 5°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

[Note—Identify the peaks using the *Relative Retention Time* values given in *Table 2*.]

Suitability requirements

Resolution: NLT 3.0 between olanzapine related compound A and olanzapine

Tailing factor: NMT 1.5 for the olanzapine peak

Relative standard deviation: NMT 2.0% from four replicate injections for the olanzapine peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Olanzapine taken:

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

r_U = peak response of each impurity 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 = concentration of Olanzapine in the *Sample solution* (mg/mL)

F = relative response factor for each impurity from *Table 2*

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Olanzapine related compound B[a]	0.3	2.3	0.10
Olanzapine related compound A[b]	0.8	2.3	0.10
Olanzapine	1.0	—	—
Chloromethyl olanzapinium chloride[c] (if present)	1.1	1.0	0.15
Any individual, unspecified impurity	—	—	0.10
Total impurities	—	—	0.4

[a] 2-Methyl-10*H*-thieno-[2,3-*b*][1,5]benzodiazepin-4[5*H*]-one.

[b] 5-Methyl-2-((2-nitrophenyl)amino)-3-thiophenecarbonitrile.

[c] 1-Chloromethyl-1-methyl-4-(2-methyl-10*H*-benzo[*b*]thieno[2,3-e][1,4]diazepin-4-yl)piperazin-1-ium chloride.

SPECIFIC TESTS

• **Water Determination,** *Method I*⟨921⟩

[Note—A suitable solvent system for water determination in ketones and aldehydes (e.g., Hydranal composite 5K-working medium K or Aquastar composite 5K-solvent KC or equivalent) is recommended.]

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards** ⟨11⟩

USP Olanzapine RS

USP Olanzapine Related Compound A RS

5-Methyl-2-((2-nitrophenyl)amino)-3-thiophenecarbonitrile.

$C_{12}H_9N_3O_2S$ 259.28

USP Olanzapine Related Compound B RS

2-Methyl-10*H*-thieno-[2,3-*b*][1,5]benzodiazepin-4[5*H*]-one.

$C_{12}H_{10}N_2OS$ 230.29

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

Topic/Question	Contact	Expert Committee
OLANZAPINE	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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