USP Fluoxetine Related Compound B RS
N-Methyl-3-phenylpropylamine.
$C_{10}H_{15}N$ 149.23
USP Olanzapine RS
10*H*-Thieno[2,3-*b*][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl.
$C_{17}H_{20}N_4S$ 312.43
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

Olanzapine Tablets

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

IDENTIFICATION
• **INFRARED ABSORPTION** ⟨**197S**⟩
Standard solution: 1 mg/mL of USP Olanzapine RS in chloroform
Sample solution: Dissolve a quantity of powdered Tablets, equivalent to 30 mg of olanzapine, in 30 mL of chloroform, and filter. Evaporate completely to dryness with the aid of a current of air. Redissolve the residue in 1 mL of chloroform.

ASSAY
• **PROCEDURE**
Buffer 1: 6.9 g/L of monobasic sodium phosphate. Adjust with phosphoric acid to a pH of 2.5.
Buffer 2: 12 g/L of sodium dodecyl sulfate in *Buffer 1*
Mobile phase: Acetonitrile and *Buffer 2* (1:1)
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: Transfer a known quantity of Tablets, equivalent to NLT 25 mg of olanzapine, to a suitable volumetric flask. Dilute with *Mobile phase* to volume, mix, and sonicate for 10 min. Centrifuge a portion of this solution, and dilute the clear supernatant with *Mobile phase* to obtain a solution containing about 0.1 mg/mL of olanzapine. [NOTE—Agitation of the flask may be necessary before sonication to prevent Tablets from adhering to the flask, making disintegration and dissolution difficult.]
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 size: 20 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—The relative retention times for olanzapine related compound A and olanzapine are 0.89 and 1.0, respectively.]
Suitability requirements
Resolution: NLT 2.0 between olanzapine and olanzapine related compound A, *System suitability solution*
Tailing factor: NMT 1.8, *Standard solution*
Relative standard deviation: NMT 2.0%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of $C_{17}H_{20}N_4S$ in the portion of Tablets taken:

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

r_U = peak response 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: 90.0%–110.0%

PERFORMANCE TESTS
• **DISSOLUTION** ⟨**711**⟩
Medium: 0.1 N hydrochloric acid; 900 mL
Apparatus 2: 50 rpm
Time: 30 min
Mobile phase: 10 g/L of ammonium acetate in a mixture of methanol and water (2:3). Adjust with hydrochloric acid to a pH of 4.0.
Standard solution: An amount, in mg, corresponding to the Tablet label claim, of USP Olanzapine RS in 1000 mL of *Medium*. Transfer 5.0 mL of this solution to a tube, and add 2.0 mL of *Mobile phase*.
Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Transfer 5.0 mL of the filtrate to a tube, and add 2.0 mL of *Mobile phase*.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 260 nm
Column: 4.6 mm × 15 cm; 5-µm packing L10
Flow rate: 1.5 mL/min
Injection size: 50 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Relative standard deviation: NMT 2.0%
Analysis
Calculate the percentage of olanzapine dissolved:

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

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)
V = volume of *Medium*, 900 mL
L = label claim (mg/Tablet)
Tolerances: NLT 80% (Q) of the labeled amount of olanzapine is dissolved.
• **UNIFORMITY OF DOSAGE UNITS** ⟨**905**⟩**:** Meet the requirements

IMPURITIES
Organic Impurities
• **PROCEDURE**
Buffer 1: 3.3 mL/L of phosphoric acid. Adjust with 50% NaOH to a pH of 2.5.
Buffer 2: 8.7 g/L of sodium dodecyl sulfate in *Buffer 1*
Buffer 3: 18.6 mg/L of edetate disodium (EDTA) in *Buffer 2*
Solution A: Acetonitrile and *Buffer 2* (12:13)
Solution B: Acetonitrile and *Buffer 2* (7:3)
Diluent: Acetonitrile and *Buffer 3* (2:3)
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: Transfer a known quantity of Tablets to a suitable volumetric flask, and dilute with *Diluent* to volume to obtain a solution containing either 375 or 500 µg/mL of olanzapine (based on the label claim). Centrifuge a portion of this solution, and use the supernatant. [NOTE—Immediate agitation of the flask may be necessary to prevent Tablets from adhering to the flask, making

dissolution and disintegration difficult. [**Caution**—Do not sonicate.] The *Sample solution* is stable for 12 h at room temperature and 48 h if refrigerated.]

Mobile phase: See the gradient table below.

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
Temperature: 35°
Flow rate: 1.5 mL/min
Injection size: 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 impurity 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 impurity from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Olanzapine RS in the *Standard solution* (µg/mL)
C_U = concentration of olanzapine in the *Sample solution* (µg/mL)
F = relative response factor for each impurity listed in *Impurity Table 1*

Acceptance criteria
Individual impurities: See *Impurity Table 1*.
Total impurities: NMT 1.5%

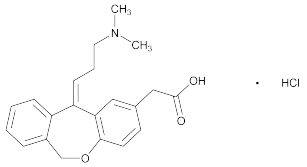
Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Olanzapine lactam[a]	0.26	1.0	0.50
Olanzapine related compound B[b]	0.30	2.3	0.20
Olanzapine thiolactam[c]	0.34	1.0	0.50
Olanzapine related compound C[d]	0.83	1.0	0.50
Olanzapine	1.0	—	—
Any individual unspecified impurity	—	1.0	0.20

[a] (*Z*)-4-(4-Methylpiperazin-1-yl)-3-(2-oxopropylidene)-1*H*-benzo[b][1,4]diazepin-2(3*H*)-one.
[b] 2-Methyl-10*H*-thieno-[2,3-*b*][1,5] benzodiazepin-4[5*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] 2-Methyl-4-(4-methylpiperazin-1-yl)-10*H*-benzo[b]thieno[2,3-e][1,4]diazepine 4′-*N*-oxide.

ADDITIONAL REQUIREMENTS
- **Packaging and Storage:** Preserve in tight, light resistant containers, and store at controlled room temperature.
- **USP Reference Standards** ⟨**11**⟩
  USP Olanzapine RS
  USP Olanzapine Related Compound A RS
  5-Methyl-2-((2-nitrophenyl)amino)-3-thiophenecarbonitrile.
  USP Olanzapine Related Compound B RS
  2-Methyl-10*H*-thieno-[2,3-b][1,5]benzodiazepin-4[5*H*]-one.
  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

Olopatadine Hydrochloride



$C_{21}H_{23}NO_3 \cdot HCl$ 373.87

Dibenz[*b,e*]oxepin-2-acetic acid, 11-[3-(dimethylamino)propylidene]-6,11-dihydro-, hydrochloride, (*Z*)-; 11-[(*Z*)-3-(Dimethylamino)propylidene]-6,11-dihydrodibenz[*b,e*]oxepin-2-acetic acid, hydrochloride [140462-76-6].

DEFINITION
Olopatadine Hydrochloride contains NLT 98.0% and NMT 102.0% of $C_{21}H_{23}NO_3 \cdot HCl$, calculated on the dried basis.

IDENTIFICATION
- **A. Infrared Absorption** ⟨**197K**⟩
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **C. Identification Tests—General,** *Chloride* ⟨**191**⟩**:** Meets the requirements

ASSAY
- **Procedure**
  [Note—Protect solutions from light.]
  Buffer: Dissolve 13.6 g of monobasic potassium phosphate in 1 L of water, add 1 mL of triethylamine, and mix. Adjust with phosphoric acid to a pH of 3.0.
  Mobile phase: Acetonitrile and *Buffer* (7:18)
  Standard solution: 0.1 mg/mL of USP Olopatadine Hydrochloride RS in *Mobile phase*
  Sample solution: 0.1 mg/mL of Olopatadine Hydrochloride in *Mobile phase*