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%

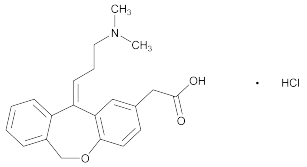
Impurity Table 1

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*

Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 299 nm
Column: 4.6-mm × 15-cm; 5-µm packing L7
Flow rate: 1 mL/min
Injection size: 30 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Column efficiency: NLT 2000 theoretical plates based on Olopatadine peak
Tailing factor: NMT 2.0
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of $C_{21}H_{23}NO_3 \cdot HCl$ in the portion of Olopatadine Hydrochloride taken:

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

r_U = peak response of the *Sample solution*
r_S = peak response of the *Standard solution*
C_S = concentration of USP Olopatadine Hydrochloride RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of Olopatadine Hydrochloride in the *Sample solution* (mg/mL)
Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

Inorganic Impurities
- **Residue on Ignition** ⟨**281**⟩**:** NMT 0.1%
- **Heavy Metals,** *Method II* ⟨**231**⟩**:** NMT 10 ppm

Organic Impurities
- **Procedure**

[Note—Protect solutions from light.]
Mobile phase: Proceed as directed in the *Assay*.
Blank solution: *Mobile phase*
System suitability solution: 0.2 mg/mL of USP Olopatadine Hydrochloride RS and 0.02 mg/mL of USP Olopatadine Related Compound B RS in *Mobile phase*
Sample solution: 0.2 mg/mL of Olopatadine Hydrochloride in *Mobile phase*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 299 nm
Column: 4.6-mm × 15-cm; 5-µm packing L7
Flow rate: 1 mL/min
Injection size: 30 µL
Run time: At least 2.5 times the retention time of the major peak
System suitability
Sample: *System suitability solution*
[Note—The relative retention times for olopatadine and olopatadine related compound B are 1.0 and 1.2, respectively.]
Suitability requirements
Resolution: NLT 2.0 between olopatadine and olopatadine related compound B
Column efficiency: NLT 2000 theoretical plates, olopatadine peak
Tailing factor: NMT 2.0, olopatadine peak
Relative standard deviation: NMT 2.0%, olopatadine peak
Analysis
Sample: *Sample solution*
Calculate the percentage of each impurity in the portion of Olopatadine Hydrochloride taken:

$$\text{Result} = (r_U/r_T) \times (1/F) \times 100$$

r_U = peak response of each individual impurity from the *Sample solution*
r_T = sum of all the peak responses from the *Sample solution*
F = relative response factor for each individual impurity (see *Impurity Table 1*)
[Note—Disregard any peaks corresponding to those of the *Blank solution*.]
Acceptance criteria
Individual impurities: See *Impurity Table 1*.
Total impurities: NMT 0.25%

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
α-Hydroxy Olopatadine[a]	0.4	1.0	0.2
Olopatadine *E*-isomer[b]	0.7	1.3	0.1
Olopatadine	1.0	—	—
Any other individual impurity	—	1.0	0.1

[a] (*Z*)-2-{11-[3-(Dimethylamino)propylidene]-6,11-dihydrodibenz[*b,e*]oxepin-2-yl}-2-hydroxyacetic acid.
[b] 11-[(*E*)-3-(Dimethylamino)propylidene]-6,11-dihydrodibenz[*b,e*]oxepin-2-acetic acid.

SPECIFIC TESTS

- **pH** ⟨**791**⟩**:** Between 2.0 and 4.0, in a solution (1 in 100)
- **Loss on Drying** ⟨**731**⟩**:** Dry a sample at 105° for 3 h: it loses NMT 0.3% of its weight.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers and store at room temperature.
- **USP Reference Standards** ⟨**11**⟩
USP Olopatadine Hydrochloride RS
USP Olopatadine Related Compound B RS
(*Z*)-3-{2-(Carboxymethyl)dibenzo[*b,e*]oxepin-11(6*H*)-ylidene}-*N*,*N*-dimethylpropan-1-amine oxide.
$C_{21}H_{23}NO_4$ 353.41

Olopatadine Hydrochloride Ophthalmic Solution

DEFINITION

Olopatadine Hydrochloride Ophthalmic Solution is a sterile aqueous solution of Olopatadine Hydrochloride. It contains NLT 90.0% and NMT 110.0% of the labeled amount of olopatadine ($C_{21}H_{23}NO_3$). It may contain suitable antimicrobial agents.

IDENTIFICATION

- 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**

[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: Equivalent to 0.1 mg/mL of olopatadine in *Mobile phase*, from Olopatadine Hydrochloride Ophthalmic Solution