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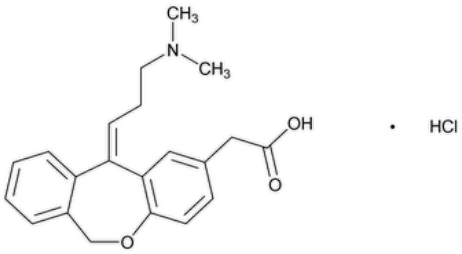
Olopatadine Hydrochloride



$C_{21}H_{23}NO_3 \cdot HCl$ 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-dihydrodibenzo[*b,e*]oxepin-2-acetic acid, hydrochloride CAS RN®: 140462-76-6; UNII: 2XG66W44KF.

DEFINITION

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

IDENTIFICATION

Change to read:

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

• **C.** **Identification Tests—General ⟨191⟩, *Chloride*:** Meets the requirements

ASSAY

• **Procedure**

Protect all solutions containing olopatadine hydrochloride 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* (28:72)

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 volume: 30 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of olopatadine hydrochloride ($C_{21}H_{23}NO_3 \cdot HCl$) in the portion of Olopatadine Hydrochloride taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Organic Impurities**

Protect all solutions containing olopatadine hydrochloride from light.

Mobile phase: Prepare as directed in the *Assay*.

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*

Blank solution: *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 volume: 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

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 *Table 1*)

Acceptance criteria

Individual impurities: See *Table 1*. Disregard any peaks corresponding to those of the *Blank solution*, and any peak less than 0.05%.

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

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Olopatadine	1.0	—	—
Any other individual impurity	—	1.0	0.1
Total impurities	—	—	0.25

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

[b] 11-[(*E*)-3-(Dimethylamino)propylidene]-6,11-dihydrodibenzo[*b*,*e*]oxepin-2-acetic acid.

SPECIFIC TESTS

- **pH** ⟨791⟩

  Sample: 10 mg/mL of Olopatadine Hydrochloride in water

  Acceptance criteria: 2.0–4.0

- **Loss on Drying** ⟨731⟩

  Analysis: Dry at 105° for 3 h.

  Acceptance criteria: NMT 0.3%

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

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

Topic/Question	Contact	Expert Committee
OLOPATADINE HYDROCHLORIDE	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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