Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-May-2017
Document Type: USP Monographs
DocId: GUID-89D616C0-FC77-4285-B4CB-148A007B5B97_1_en-US
DOI: https://doi.org/10.31003/USPNF_M3312_01_01
DOI Ref: l5ppb

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

• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

• **B.** The UV spectrum in the range of 270–370 nm of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

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: Nominally equivalent to 0.1 mg/mL of olopatadine in *Mobile phase*, from Ophthalmic Solution

Chromatographic system

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

Mode: LC

Detector: UV 299 nm or diode array. [Note—Use a diode array detector to perform the *Identification B* test.]

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 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of olopatadine ($C_{21}H_{23}NO_3$) in the portion of Ophthalmic Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

M_{r1} = molecular weight of olopatadine, 337.41

M_{r2} = molecular weight of olopatadine hydrochloride, 373.87

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• Limit of Early Eluting 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*

Standard solution: 0.2 mg/mL of USP Olopatadine Hydrochloride RS in *Mobile phase*

Sample solution: Equivalent to 0.2 mg/mL of olopatadine in *Mobile phase*, from Ophthalmic Solution

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 1.6 times the retention time of the major peak

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between olopatadine and olopatadine related compound B, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Ophthalmic Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

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

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

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

M_{r1} = molecular weight of olopatadine, 337.41

M_{r2} = molecular weight of olopatadine hydrochloride, 373.87

F = relative response factor for each individual impurity (see *Table 1*)

Acceptance criteria: See *Table 1*. Disregard any peaks corresponding to those of the *Blank solution* and any peaks with a relative retention time, measured with respect to olopatadine, greater than 1.5. Disregard any peak less than 0.1%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Olopatadine *E*-isomer[a]	0.7	1.3	0.5
Olopatadine	1.0	—	—
Olopatadine related compound B	1.2	1.0	2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Olopatadine carbaldehyde[b]	1.3	4.5	0.5
Any individual unspecified impurity	—	1.0	0.5

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

[b] (*Z*)-11-[3-(Dimethylamino)propylidene]-6,11-dihydrodibenzo[*b*,*e*]oxepine-2-carbaldehyde.

• **Limit of Late Eluting Impurities**

Protect all solutions containing olopatadine hydrochloride from light.

Buffer: Prepare as directed in the *Assay*.

Mobile phase: Acetonitrile and *Buffer* (1:1)

System suitability solution: 0.02 mg/mL of USP Olopatadine Hydrochloride RS and 0.01 mg/mL of USP Olopatadine Related Compound C RS in *Mobile phase*

Standard solution: 0.01 mg/mL of USP Olopatadine Related Compound C RS in *Mobile phase*

Sample solution: Use the *Sample solution* from the test for *Limit of Early Eluting Impurities*.

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 3 times the retention time of the olopatadine related compound C peak

System suitability

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

[Note—The relative retention times for olopatadine and olopatadine related compound C are 0.3 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 7.0 between olopatadine and olopatadine related compound C, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Ophthalmic Solution taken:

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

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of olopatadine related compound C from the *Standard solution*

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

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

Acceptance criteria: See *Table 2*. Disregard any peaks corresponding to those of the *Blank solution* and any peaks with a relative retention time, measured with respect to olopatadine related compound C, less than 0.7. Disregard any peak less than 0.1%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Olopatadine	0.3	—

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Olopatadine related compound C	1.0	1
Any individual unspecified impurity	—	0.5
Total impurities[a]	—	3

[a] Total impurities are the sum of olopatadine related compound B, olopatadine related compound C, olopatadine *E*-isomer, olopatadine carbaldehyde, and all unspecified impurities found in the tests for *Limit of Early Eluting Impurities* and *Limit of Late Eluting Impurities*.

SPECIFIC TESTS

- **Sterility Tests ⟨71⟩:** Meets the requirements
- **pH ⟨791⟩:** 5.0–8.0
- **Osmolality and Osmolarity ⟨785⟩:** 260–340 mOsmol/kg

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers. Store between 4° and 25°.
- **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

USP Olopatadine Related Compound C RS

11-Oxo-6,11-dihydrodibenzo[*b*,*e*]oxepin-2-yl acetic acid.

$C_{16}H_{12}O_4$ 268.26

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

Topic/Question	Contact	Expert Committee
OLOPATADINE HYDROCHLORIDE OPHTHALMIC SOLUTION	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 42(1)

Current DocID: GUID-89D616C0-FC77-4285-B4CB-148A007B5B97_1_en-US

DOI: https://doi.org/10.31003/USPNF_M3312_01_01

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