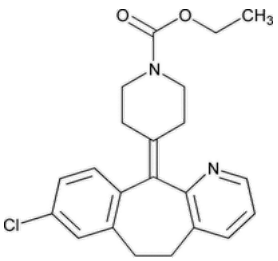
Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-D0D2BB6E-7D09-4246-A466-C267AFABE90D_4_en-US
DOI: https://doi.org/10.31003/USPNF_M45894_04_01
DOI Ref: n1wen

Loratadine



$C_{22}H_{23}ClN_2O_2$ 382.88

1-Piperidinecarboxylic acid, 4-(8-chloro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)-, ethyl ester;

Ethyl 4-(8-chloro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)-1-piperidinecarboxylate CAS RN®: 79794-75-5; UNII: 7AJO3BO7QN.

DEFINITION

Loratadine contains NLT 98.5% and NMT 101.0% of loratadine ($C_{22}H_{23}ClN_2O_2$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197M**▲ (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 A (0.01 M dibasic potassium phosphate)**:** 1.74 g/L of anhydrous dibasic potassium phosphate in water

Buffer B (0.6 M dibasic potassium phosphate)**:** 105 g/L of anhydrous dibasic potassium phosphate in water

0.05 N hydrochloric acid: Transfer 500 mL of water to a 1000-mL volumetric flask, add 83 mL of hydrochloric acid, and dilute with water to volume. Transfer 50 mL of this solution into a 1000-mL volumetric flask, and dilute with water to volume.

Mobile phase: Acetonitrile, methanol, and *Buffer A* (60:60:70). Adjust with 10% phosphoric acid to an apparent pH of 7.2.

Diluent: Transfer 400 mL of *0.05 N hydrochloric acid* and 80 mL of *Buffer B* to a 1-L volumetric flask. Dilute with a mixture of acetonitrile and methanol (1:1) to volume.

Standard solution: 0.4 mg/mL of USP Loratadine RS in *Diluent*

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

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

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

Column temperature: 25°–35°

Flow rate: 1 mL/min

Injection volume: 15 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of loratadine ($C_{22}H_{23}ClN_2O_2$) in the portion of Loratadine 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 Loratadine RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.5%–101.0% on the dried basis

IMPURITIES

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

• **Organic Impurities, Procedure 1**

[Note—On the basis of the synthetic route, perform either *Procedure 1* or *Procedure 2*. *Procedure 2* is recommended if 4,8-dichloro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-one is a potential related compound.]

Mobile phase and **Diluent:** Proceed as directed in the *Assay*.

Standard solution: 0.8 µg/mL of USP Loratadine RS in *Diluent*

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

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

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

Column temperature: 25°–35°

Flow rate: 1 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 4.0%

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

r_S = peak area of loratadine from the *Standard solution*

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

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

F = relative response factor as listed in *Table 1*

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Fluoroloratadine[a]	0.79	0.25	0.2
Loratadine	1.0	—	—
Any other individual impurity	—	1.0	0.1
Total impurities	—	—	0.3

[a] Ethyl 4-(8-chloro-11-fluoro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-yl) piperidin-1-carboxylate.

• **Organic Impurities, Procedure 2**

Solution A: Dissolve 0.96 g of 1-pentanesulfonic acid sodium salt in 900 mL of water. Adjust with phosphoric acid solution (1 in 10) to a pH of 3.00 ± 0.05, and dilute with water to 1 L.

Solution B: Acetonitrile

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	75	25
20	50	50
30	40	60
35	30	70
45	30	70
50	75	25

Standard stock solution: 0.1 mg/mL each of USP Loratadine RS, USP Loratadine Related Compound A RS, and USP Loratadine Related Compound B RS in methanol

Standard solution: 0.01 mg/mL each of USP Loratadine RS, USP Loratadine Related Compound A RS, and USP Loratadine Related Compound B RS prepared as follows. Transfer 1.0 mL of the *Standard stock solution* to a 10-mL volumetric flask, add 2 mL of *Solution A*, and dilute with methanol to volume.

Sample solution: 10 mg/mL of Loratadine prepared as follows. Transfer 100 mg of Loratadine to a 10-mL volumetric flask, and dissolve in 2 mL of methanol. Add 2 mL of *Solution A*, and then dilute with methanol to volume.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1.2 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 1.5 between loratadine related compound A and loratadine related compound B

Relative standard deviation: NMT 10% for the loratadine peak

Analysis

Sample: *Sample solution*

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

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

r_U = peak area of each individual impurity from the *Sample solution*

r_S = peak area of loratadine from the *Standard solution*

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

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

F = relative response factor as listed in *Table 3*

Acceptance criteria: See *Table 3*.

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Loratadine related compound A	0.50	1.00	0.1
Loratadine related compound B	0.53	0.89	0.1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Loratadine related compound C[a]	0.70	0.60	0.1
Hydroxy deacyl analog[b]	0.75	0.46	0.1
Loratadine	1.00	—	—
Dichlorobenzocycloheptapyridinone[c]	1.23	0.92	0.1
Hydroxyloratadine[d]	1.60	0.42	0.1
4-Chloroloratadine[e]	1.83	1.08	0.1
Any individual unknown impurity	—	1.0	0.10
Total impurities	—	—	0.3

[a] 8-Chloro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-one.

[b] 8-Chloro-5,6-dihydro-11-hydroxy-11-(1-methylpiperidin-4-yl)-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine.

[c] 4,8-Dichloro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-one.

[d] Ethyl 4-(8-chloro-11-hydroxy-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-yl) piperidin-1-carboxylate.

[e] Ethyl 4-(4,8-dichloro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidin-1-carboxylate.

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry a sample at 100° to constant weight.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers, and store between 2° and 30°.

• **Labeling:** If a test for *Organic Impurities* other than *Procedure 1* is used, then the labeling states with which *Organic Impurities* test the article complies.

• **USP Reference Standards ⟨11⟩**

USP Loratadine RS

USP Loratadine Related Compound A RS

8-Chloro-5,6-dihydro-11-(piperidin-4-ylidene)-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine.

$C_{19}H_{19}ClN_2$ 310.82

USP Loratadine Related Compound B RS

8-Chloro-5,6-dihydro-11-(*N*-methylpiperidin-4-ylidene)-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine.

$C_{20}H_{21}ClN_2$ 324.85

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

Topic/Question	Contact	Expert Committee
LORATADINE	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 38(5)

Current DocID: GUID-D0D2BB6E-7D09-4246-A466-C267AFABE90D_4_en-US

DOI: https://doi.org/10.31003/USPNF_M45894_04_01

DOI ref: n1wen