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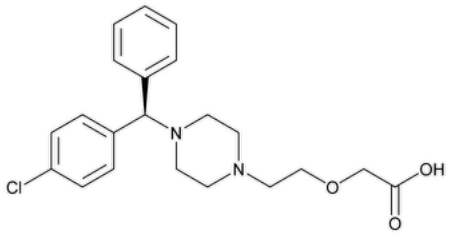
Levocetirizine Dihydrochloride



• 2 HCl

$C_{21}H_{25}ClN_2O_3 \cdot 2HCl$ 461.81

Acetic acid, [2-[4-[(*R*)-(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]-, dihydrochloride;

(2-{4-[(*R*)-(4-Chlorophenyl)phenylmethyl]piperazin-1-yl}ethoxy)acetic acid dihydrochloride CAS RN®: 130018-87-0.

Levocetirizine free base

$C_{21}H_{25}ClN_2O_3$ 388.89 CAS RN®: 130018-77-8.

DEFINITION

Levocetirizine Dihydrochloride contains NLT 98.0% and NMT 102.0% of levocetirizine dihydrochloride ($C_{21}H_{25}ClN_2O_3 \cdot 2HCl$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the levocetirizine peak of the *System suitability solution*, as obtained in the test for *Enantiomeric Purity*.

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

ASSAY

• **Procedure**

Mobile phase: Acetonitrile, water, and 1 M sulfuric acid TS (93: 6.6: 0.4)

Standard solution: 0.05 mg/mL of USP Levocetirizine Dihydrochloride RS in *Mobile phase*

Sample solution: 0.05 mg/mL of Levocetirizine Dihydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 25-cm; 5-µm packing L3

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of levocetirizine dihydrochloride ($C_{21}H_{25}ClN_2O_3 \cdot 2HCl$) in the portion of Levocetirizine Dihydrochloride taken:

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

r_U = peak response of levocetirizine from the *Sample solution*

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

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

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

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

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.2%
- **Organic Impurities**

Mobile phase: Acetonitrile, water, and 1 M sulfuric acid TS (93:6.6:0.4)

System suitability solution: 0.2 mg/mL of USP Levocetirizine Dihydrochloride RS and 0.2 µg/mL each of USP Levocetirizine Amide RS and USP Chlorobenzhydryl Piperazine RS in *Mobile phase*. Use the solution within 16 h.

Standard solution: 0.2 µg/mL each of USP Levocetirizine Dihydrochloride RS, USP Levocetirizine Amide RS, and USP Chlorobenzhydryl Piperazine RS in *Mobile phase*. Use the solution within 16 h.

Sample solution: 200 µg/mL of Levocetirizine Dihydrochloride in *Mobile phase*. Use the solution within 16 h.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 25-cm; 5-µm packing L3

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 3 times the retention time of levocetirizine

System suitability

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

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 3.0 between levocetirizine and chlorobenzhydryl piperazine, *System suitability solution*

Tailing factor: NMT 2.0 for levocetirizine, *System suitability solution*

Relative standard deviation: NMT 5.0% for levocetirizine, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of levocetirizine amide or chlorobenzhydryl piperazine in the portion of Levocetirizine Dihydrochloride taken:

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

r_U = peak response of levocetirizine amide or chlorobenzhydryl piperazine from the *Sample solution*

r_S = peak response of levocetirizine amide or chlorobenzhydryl piperazine from the *Standard solution*

C_S = concentration of USP Levocetirizine Amide RS or USP Chlorobenzhydryl Piperazine RS in the *Standard solution* (µg/mL)

C_U = concentration of Levocetirizine Dihydrochloride in the *Sample solution* (µg/mL)

Calculate the percentage of any unspecified impurity in the portion of Levocetirizine Dihydrochloride taken:

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

r_U = peak response of any unspecified impurity from the *Sample solution*

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

C_S = concentration of USP Levocetirizine Dihydrochloride RS in the *Standard solution* (µg/mL)

C_U = concentration of Levocetirizine Dihydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Levocetirizine	1.0	—
Chlorobenzhydryl piperazine	1.3	0.2
Levocetirizine amide	2.5	0.2
Any individual unspecified impurity	—	0.1
Total impurities	—	0.5

• **Enantiomeric Purity**

Protect solutions containing levocetirizine from direct exposure to light.

Buffer: 1.5 g/L of ammonium acetate in water. Adjust with glacial acetic acid to a pH of 4.8.

Mobile phase: Acetonitrile and *Buffer* (30:70)

System suitability solution: 0.5 mg/mL of USP Cetirizine Hydrochloride RS in water

Sample solution: 0.5 mg/mL of Levocetirizine Dihydrochloride in water

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 25-cm; 5-µm packing L90. [Note—A suitable guard column may be used.]

Column temperature: 30°

Flow rate: 0.5 mL/min

Injection volume: 20 µL

Run time: NLT 1.8 times the retention time of levocetirizine

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for the *S*-enantiomer (of cetirizine) and levocetirizine, which is the *R*-enantiomer (of cetirizine), are about 0.83 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.4 between the *S*-enantiomer and levocetirizine

Tailing factor: NMT 2.0 for levocetirizine

Relative standard deviation: NMT 1.5% each for levocetirizine and the *S*-enantiomer

Analysis

Sample: *Sample solution*

Calculate the percentage of the *S*-enantiomer in the portion of Levocetirizine Dihydrochloride taken:

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

r_U = peak response of the *S*-enantiomer from the *Sample solution*

r_T = sum of the peak responses of the *S*-enantiomer and levocetirizine from the *Sample solution*

Acceptance criteria: NMT 2.0% of the *S*-enantiomer

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° to constant weight.

Acceptance criteria: NMT 1.0%

• **pH ⟨791⟩**

Sample solution: 50 mg/mL of Levocetirizine Dihydrochloride in water

Acceptance criteria: 1.2–1.8

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers, protected from light at controlled room temperature.

• **USP Reference Standards ⟨11⟩**

USP Cetirizine Hydrochloride RS

USP Chlorobenzhydryl Piperazine RS

(*R*)-1-[(4-Chlorophenyl)phenylmethyl]piperazine.

$C_{17}H_{19}ClN_2$ 286.80

USP Levocetirizine Amide RS

(*R*)-2-(2-{4-[(4-Chlorophenyl)phenylmethyl]piperazin-1-yl}ethoxy)acetamide.

$C_{21}H_{26}ClN_3O_2$ 387.90

USP Levocetirizine Dihydrochloride RS

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

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

Chromatographic Database Information: Chromatographic Database

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