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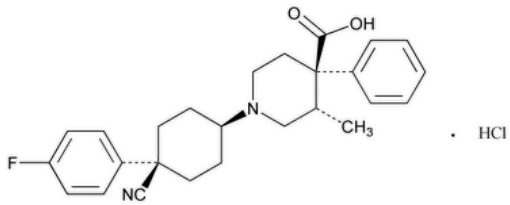
Levocabastine Hydrochloride



$C_{26}H_{29}FN_2O_2 \cdot HCl$ 456.98

4-Piperidinecarboxylic acid, 1-[4-cyano-4-(4-fluorophen yl)cyclohexyl]-3-methyl-4-phenyl-, monohydrochloride, (−)-[1(*cis*),3α,4β]-; (−)-*trans*-1-[*cis*-4-Cyano-4-(*p*-fluorophenyl)cyclohexyl]-3-methyl-4-phenylisonipecotic acid monohydrochloride CAS RN®: 79547-78-7; UNII: 124XMA6YEI.

DEFINITION

Levocabastine Hydrochloride contains NLT 98.5% and NMT 101.5% of $C_{26}H_{29}FN_2O_2 \cdot HCl$, calculated on the dried basis.

IDENTIFICATION

Change to read:

- **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)
- **B. Identification Tests—General, *Chloride*⟨191⟩:** Meets the requirements
- **C. Optical Rotation, *Specific Rotation*⟨781S⟩:** Meets the requirements

ASSAY

- **Procedure**

Sample solution: Dissolve 175 mg of Levocabastine Hydrochloride in 50 mL of alcohol, and add 5.0 mL of 0.01 N hydrochloric acid.

Titrimetric system

(See *Titrimetry* ⟨541⟩.)

Mode: Direct titration

Titrant: 0.1 N sodium hydroxide VS

Endpoint detection: Potentiometric

Analysis

Sample: *Sample solution*

The volume of titrant required to titrate Levocabastine Hydrochloride is the difference between the first and third endpoints. Perform a blank determination and make any necessary correction. Each mL of 0.1 N sodium hydroxide VS is equivalent to 22.85 mg of $C_{26}H_{29}FN_2O_2 \cdot HCl$.

Acceptance criteria: 98.5%–101.5% on the dried basis

IMPURITIES

Inorganic Impurities

- **Residue on Ignition ⟨281⟩:** NMT 0.1%, based on a sample weight of about 1.000 g

Organic Impurities

- **Procedure**

[Note—Prepare solutions immediately before use.]

Diluent: 2 mg/mL of sodium hydroxide in water

Solution A: Dissolve 1.39 g of boric acid in water, and adjust with 1 N sodium hydroxide to a pH of 9.0. Dilute with water to 100 mL.

Run buffer: Dissolve 1.08 g of sodium dodecyl sulfate and 650 mg of hydroxypropyl-β-cyclodextrin in 5 mL of isopropyl alcohol, then dilute with *Solution A* to 50 mL.

System suitability solution: 12.5 µg/mL of USP Levocabastine Hydrochloride RS and 12.5 µg/mL of USP Levocabastine Related Compound A RS in *Diluent*

Standard solution: Dilute 5.0 mL of the *Sample solution* with *Diluent* to 100 mL. Dilute 1.0 mL of this solution with *Diluent* to 10 mL to obtain a solution containing 12.5 µg/mL of Levocabastine Hydrochloride.

Sample solution: 2.5 mg/mL of Levocabastine Hydrochloride in *Diluent*

Capillary electrophoresis system

Detector: UV 214 nm

Column: 75-µm × 50-cm uncoated fused-silica capillary column

Column temperature: 50°

Current: See the gradient table below.

Time (min)	Current (µA)
0	0
0.17	75
15	130
40	130
60	200

[Note—Before performing the *System suitability*, equilibrate the capillary column with *Diluent* for 2 min, then equilibrate with *Run buffer* for at least 5 min.]

System suitability

Sample: *System suitability solution*

[Note—The relative migration times for levocabastine and levocabastine related compound A are approximately 1.0 and 1.07, respectively.]

Suitability requirements

Resolution: NLT 4 between levocabastine and levocabastine related compound A

[Note—If necessary, adjust the current gradient to achieve the required resolution.]

Analysis

Samples: *Diluent* (blank), *Standard solution*, and *Sample solution*

Separately inject equal volumes (pressure of 3450 Pa for 5 s) of the *Samples*, and record the peak responses.

[Note—Disregard any peak originating from the *Diluent*. Disregard any peak with an area of less than 0.1 times the major peak area of the *Standard solution* (0.05%).]

Acceptance criteria: The area for any peak in the *Sample solution*, other than the major peak, is not greater than the major peak area of the *Standard solution* (0.5%); and the sum of all peak areas in the *Sample solution*, except for the major peak, is not greater than twice the major peak area of the *Standard solution* (1.0%).

SPECIFIC TESTS

- **Optical Rotation, *Specific Rotation*⟨781S⟩:** −102° to −106° at 20°

  Sample solution: 10 mg/mL in methanol
- **Loss on Drying ⟨731⟩:** Dry about 1.000 g of the sample at 105° to constant weight: it loses NMT 0.5% of its weight.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers. Protect from light.
- **USP Reference Standards ⟨11⟩**

  USP Levocabastine Hydrochloride RS

  USP Levocabastine Related Compound A RS

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

Topic/Question	Contact	Expert Committee
LEVOCABASTINE HYDROCHLORIDE	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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