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Lidocaine Hydrochloride

$C_{14}H_{22}N_2O \cdot HCl \cdot H_2O$ 288.81
Acetamide, 2-(diethylamino)-*N*-(2,6-dimethylphenyl)-, monohydrochloride, monohydrate;
2-(Diethylamino)-2',6'-acetoxylidide monohydrochloride monohydrate CAS RN®: 6108-05-0; UNII: V13007Z41A.
Anhydrous 270.80 CAS RN®: 73-78-9; UNII: EC2CNF7XFP.

DEFINITION
Lidocaine Hydrochloride contains NLT 97.5% and NMT 102.5% of lidocaine hydrochloride ($C_{14}H_{22}N_2O \cdot HCl$), calculated on the anhydrous basis.

IDENTIFICATION
Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*.**▲ (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, *Chloride*⟨191⟩:** Meets the requirements

ASSAY
• **Procedure**

Solution A: Water and glacial acetic acid (930:50). Adjust with 1 N sodium hydroxide to a pH of 3.40.

Mobile phase: Acetonitrile and *Solution A* (1:4)

Standard solution: 2.0 mg/mL of USP Lidocaine Hydrochloride RS in *Mobile phase*

System suitability stock solution: 220 µg/mL of methylparaben in *Mobile phase*

System suitability solution: Mix 2 mL of *System suitability stock solution* and 20 mL of *Standard solution*.

Sample solution: 2 mg/mL of Lidocaine Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; packing L1

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 3.0 between lidocaine and methylparaben, *System suitability solution*

Relative standard deviation: NMT 1.5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of lidocaine hydrochloride ($C_{14}H_{22}N_2O \cdot HCl$) in the portion of Lidocaine 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 Lidocaine Hydrochloride RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 97.5%–102.5% on the anhydrous basis

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

• **Chloride and Sulfate, *Sulfate*⟨221⟩**

Sample: 100 mg

Analysis: Dissolve *Sample* in 10 mL of water, and add 1 mL of 3 N hydrochloric acid. Mix, and add 1 mL of barium chloride TS.

Acceptance criteria: The turbidity does not exceed that produced by 0.10 mL of 0.020 N sulfuric acid (NMT 0.1%).

- **Organic Impurities**

Buffer: 4.85 g/L of monobasic potassium phosphate in water. Adjust with sodium hydroxide solution to a pH of 8.0.

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

Standard solution: 0.5 µg/mL of USP Ropivacaine Related Compound A RS and 5 µg/mL each of USP Lidocaine Related Compound H RS and USP Lidocaine Hydrochloride RS in *Mobile phase*

Sample solution: 5 mg/mL of Lidocaine Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 3.9-mm × 15-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 3.5 times the retention time for lidocaine

System suitability

Sample: *Standard solution*

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

Suitability requirements

Resolution: NLT 1.5 between lidocaine related compound H and ropivacaine related compound A; NLT 2.0 between ropivacaine related compound A and lidocaine

Relative standard deviation: NMT 10.0% for ropivacaine related compound A

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of lidocaine related compound H or ropivacaine related compound A in the portion of Lidocaine Hydrochloride taken:

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

r_U = peak response for lidocaine related compound H or ropivacaine related compound A from the *Sample solution*

r_S = peak response of lidocaine related compound H or ropivacaine related compound A from the *Standard solution*

C_S = concentration of USP Lidocaine Related Compound H RS or USP Ropivacaine Related Compound A RS in the *Standard solution* (µg/mL)

C_U = concentration of Lidocaine Hydrochloride in the *Sample solution* (µg/mL)

Calculate the percentage of any individual unspecified impurity in the portion of Lidocaine Hydrochloride taken:

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

r_U = peak response for each unspecified impurity from the *Sample solution*

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

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

C_U = concentration of Lidocaine Hydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Lidocaine related compound H	0.38	0.10
Ropivacaine related compound A	0.42	0.01

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Lidocaine	1.0	—
Any individual unspecified impurity	—	0.10
Total impurities	—	0.5

SPECIFIC TESTS

• **Water Determination,** *Method I*⟨921⟩**:** 5.0%–7.0%

• **Sterility Tests** ⟨71⟩**:** Where the label states that Lidocaine Hydrochloride is sterile, it meets the requirements.

• **Bacterial Endotoxins Test** ⟨85⟩**:** Where the label states that Lidocaine Hydrochloride is sterile or must be subjected to further processing during the preparation of injectable dosage forms, it contains NMT 1.1 USP Endotoxin Units/mg of lidocaine hydrochloride.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.

• **Labeling:** Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

• **USP Reference Standards** ⟨11⟩

USP Lidocaine Hydrochloride RS

USP Lidocaine Related Compound H RS

2-Chloro-*N*-(2,6-dimethylphenyl)acetamide.

$C_{10}H_{12}ClNO$ 197.66

USP Ropivacaine Related Compound A RS

2,6-Dimethylaniline hydrochloride.

$C_8H_{11}N \cdot HCl$ 157.64

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

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

Chromatographic Database Information: Chromatographic Database

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