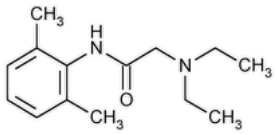
Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-Apr-2024
Document Type: USP Monographs
DocId: GUID-D615982A-5B73-4FCC-8A33-B96A726A9D37_8_en-US
DOI: https://doi.org/10.31003/USPNF_M45070_08_01
DOI Ref: q3vdf

Lidocaine



$C_{14}H_{22}N_2O$ 234.34

Acetamide, 2-(diethylamino)-*N*-(2,6-dimethylphenyl)-;

2-(Diethylamino)-2',6'-acetoxylidide CAS RN®: 137-58-6; UNII: 98PI200987.

DEFINITION

Lidocaine contains NLT 97.5% and NMT 102.5% of lidocaine ($C_{14}H_{22}N_2O$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K** [Note—Methods described under ⟨197K⟩ or ⟨197A⟩ may be used.]

Sample: Previously dried under vacuum over silica gel for 24 h

Acceptance criteria: Meets the requirements

• **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

Change to read:

• **Procedure**

Solution A: Water and glacial acetic acid (930:50). Adjust with 1 N sodium hydroxide to a pH of 3.4.

Mobile phase: Acetonitrile and *Solution A* (20:80)

Standard solution: 1.7 mg/mL of USP Lidocaine RS in *Mobile phase*, prepared as follows. Dissolve 85 mg of USP Lidocaine RS with 0.5 mL of 1 N hydrochloric acid, warming if necessary, in a 50-mL flask. Dilute with *Mobile phase* to volume.

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: 1.7 mg/mL of Lidocaine in *Mobile phase*, prepared as follows. Dissolve 85 mg of Lidocaine with 0.5 mL of 1 N hydrochloric acid, warming if necessary, in a 50-mL flask. Dilute with *Mobile phase* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; ▲10-µm▲ (ERR 1-Apr-2024) 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 ($C_{14}H_{22}N_2O$) in the portion of Lidocaine taken:

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

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

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

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

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

Acceptance criteria: 97.5%–102.5%

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Chloride and Sulfate ⟨221⟩, *Chloride***

Sample: 1.0 g

Analysis: Dissolve the *Sample* in a mixture of 3 mL of 2 N nitric acid and 12 mL of water, and add 1 mL of silver nitrate TS.

Acceptance criteria: The turbidity does not exceed that produced by 50 µL of 0.020 N hydrochloric acid (NMT 0.0035%).

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

Sample: 100 mg

Analysis: Dissolve the *Sample* in a mixture of 1 mL of 2 N nitric acid and 10 mL of water. Filter if necessary, 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**

Solution A: 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 *Solution A* (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 RS in *Mobile phase*

Sample solution: 5 mg/mL of Lidocaine 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

System suitability

Sample: *Standard solution*

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

Suitability requirements

Resolution: NLT 1.5 between the lidocaine related compound H and 2,6-dimethylaniline (ropivacaine related compound A free base) peaks

Relative standard deviation: NMT 10.0% for 2,6-dimethylaniline

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of lidocaine related compound H in the portion of Lidocaine taken:

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

r_U = peak response of lidocaine related compound H from the *Sample solution*

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

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

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

Calculate the percentage of 2,6-dimethylaniline (ropivacaine related compound A free base) in the portion of Lidocaine taken:

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

r_U = peak response of 2,6-dimethylaniline from the *Sample solution*

r_S = peak response of 2,6-dimethylaniline from the *Standard solution*

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

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

M_{r1} = molecular weight of 2,6-dimethylaniline, 121.18

M_{r2} = molecular weight of ropivacaine related compound A, 157.64

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

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

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

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

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

C_U = concentration of Lidocaine 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
2,6-Dimethylaniline	0.42	0.01
Lidocaine	1.0	—
Any unspecified impurity	—	0.10
Total impurities	—	0.5

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers. Store at room temperature.
- **USP Reference Standards** ⟨11⟩

USP Lidocaine 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	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 43(3)

Current DocID: GUID-D615982A-5B73-4FCC-8A33-B96A726A9D37_8_en-US

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