Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-May-2022
Document Type: USP Monographs
DocId: GUID-78197E6C-1F9F-4003-95CB-B1D66570D358_2_en-US
DOI: https://doi.org/10.31003/USPNF_M45080_02_01
DOI Ref: ao1g2

Lidocaine Topical Aerosol

Change to read:

DEFINITION

Lidocaine Topical Aerosol is a solution of Lidocaine in a suitable flavored vehicle with suitable propellants in a pressurized container. ▲▲ (USP 1-May-2022) It contains NLT 90.0% and NMT 110.0% of the labeled amount of lidocaine ($C_{14}H_{22}N_2O$).

▲[Note—This monograph may not be sufficient for products defined under 21 CFR Part 348.3(a).]▲ (USP 1-May-2022)

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests** ⟨197⟩, *Infrared Spectroscopy*: 197A or 197K▲ (USP 1-May-2022)

Sample: ▲Collect 10 mL of Topical Aerosol in a separator, add 10 mL of 1 N hydrochloric acid, and wash with 10 mL of hexane. Allow the two layers to completely separate. Discard the bead-like globules and the hexane wash. Collect the aqueous layer. Add 5 mL of ammonium hydroxide to the collected aqueous layer, and extract with 10 mL of hexane. Filter the hexane extract through a pledget of cotton previously moistened with hexane. Evaporate the extract to dryness under ambient conditions over molecular sieves.

Standard: Dissolve 10 mg of USP Lidocaine RS with about 2 mL of hexane. Evaporate to dryness under ambient conditions.▲ (USP 1-May-2022)

Acceptance criteria: ▲The attenuated total reflection or▲ (USP 1-May-2022) a potassium bromide dispersion of the ▲*Sample*▲ (USP 1-May-2022) exhibits maxima only at the same wavelengths as those of ▲the *Standard*.▲ (USP 1-May-2022)

Change to read:

• **B.** ▲The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2022)

Delete the following:

▲• **C.**

Analysis: To 2 mL of Aerosol spray, collected in a test tube, add 5 mL of water, 1 mL of 2 N nitric acid, and 3 mL of mercuric nitrate TS.

Acceptance criteria: A light yellow color develops (lidocaine).▲ (USP 1-May-2022)

ASSAY

Change to read:

• **Procedure**

▲**Solution A:** 0.1% (v/v) phosphoric acid in water

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
2	90	10
30	10	90
30.1	90	10
35	90	10

Diluent: Acetonitrile and water (25:75)

Standard solution: 0.04 mg/mL of USP Lidocaine RS in *Diluent*. Sonicate to dissolve if necessary.

Sample solution: Nominally 0.04 mg/mL of lidocaine in *Diluent* from a portion of Topical Aerosol. Sonicate to dissolve if necessary.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 28°

Flow rate: 0.8 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lidocaine ($C_{14}H_{22}N_2O$) in the portion of Topical Aerosol 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 = nominal concentration of lidocaine in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0% ▲(USP 1-May-2022)

PERFORMANCE TESTS

Change to read:

• ▲▲(USP 1-May-2022) **Topical Aerosols ⟨603⟩:** Meets the requirements

▲▲(USP 1-May-2022)

IMPURITIES

Add the following:

▲• **Organic Impurities**

Solution A, Solution B, Mobile phase, Diluent, and **Chromatographic system:** Proceed as directed in the *Assay*.

Sensitivity solution: 0.1 µg/mL of USP Lidocaine RS and 0.13 µg/mL of USP Ropivacaine Related Compound A RS (equivalent to 0.1 µg/mL of 2,6-dimethylaniline) in *Diluent*

Standard solution: 0.2 µg/mL of USP Lidocaine RS and 0.26 µg/mL of USP Ropivacaine Related Compound A RS (equivalent to 0.2 µg/mL of 2,6-dimethylaniline) in *Diluent*

Sample solution: Nominally 0.1 mg/mL of lidocaine in *Diluent* from Topical Aerosol. Sonicate to dissolve if necessary.

System suitability

Samples: *Sensitivity solution* and *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for lidocaine and 2,6-dimethylaniline, *Standard solution*

Relative standard deviation: NMT 5.0% for lidocaine and 2,6-dimethylaniline, *Standard solution*

Signal-to-noise ratio: NLT 10 for lidocaine and 2,6-dimethylaniline, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of 2,6-dimethylaniline (ropivacaine related compound A free base) in the portion of Topical Aerosol 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 = nominal 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 degradation product in the portion of Topical Aerosol taken:

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

r_U = peak response of any unspecified degradation product 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 = nominal concentration of lidocaine in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.1%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
2,6-Dimethylaniline	0.8	0.2
Lidocaine	1.0	—
Lidocaine related compound H[a]	1.5	—
Any unspecified degradation product	—	0.2
Total degradation products	—	2.0

[a] 2-Chloro-*N*-(2,6-dimethylphenyl)acetamide. Process impurity included in the table for identification only.

▲ (USP 1-May-2022)

SPECIFIC TESTS

Change to read:

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** ▲The total aerobic microbial count does not exceed 10^2 cfu/mL, and the total combined molds and yeasts count does not exceed 10 cfu/mL. ▲ (USP 1-May-2022) It meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in nonreactive aerosol containers. ▲Do not store at a temperature above 49°.▲ (USP 1-May-2022)

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Lidocaine RS

▲ USP Ropivacaine Related Compound A RS

2,6-Dimethylaniline hydrochloride.

$C_8H_{12}N \cdot HCl$ 157.64▲ (USP 1-May-2022)

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 46(2)

Current DocID: GUID-78197E6C-1F9F-4003-95CB-B1D66570D358_2_en-US

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