

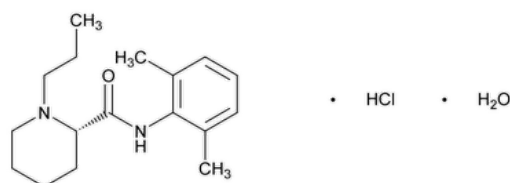
Status: Currently Official on 16-Feb-2025
 Official Date: Official as of 24-Feb-2021
 Document Type: USP Monographs
 DocId: GUID-66AB9059-EFBC-48BA-BEA9-42147E2AFD32_6_en-US
 DOI: https://doi.org/10.31003/USPNF_M73925_06_01
 DOI Ref: 2a0t2

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Ropivacaine Hydrochloride

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Change to read:



$C_{17}H_{26}N_2O \cdot HCl \cdot H_2O$ 328.88

(S)-(-)-1-Propylpiperidine-2-carboxylic acid (2,6-dimethylphenyl)amide hydrochloride monohydrate;

(S)-(-)-1-Propyl-2',6'-pipecoloxylidine hydrochloride monohydrate CAS RN®: 132112-35-7.

UNII: V910P86109.

$\Delta C_{17}H_{26}N_2O \cdot HCl$ 310.86

(S)-N-(2,6-Dimethylphenyl)-1-propylpiperidine-2-carboxamide hydrochloride CAS RN®: 98717-15-8.

UNII: 35504LBE2T.▲ (RB 24-Feb-2021)

DEFINITION

Ropivacaine Hydrochloride contains NLT 98.5% and NMT 101.0% of $C_{17}H_{26}N_2O \cdot HCl$, calculated on the anhydrous basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K
- **B. IDENTIFICATION TESTS—GENERAL (191), Chemical Identification Tests, Chloride**

Sample solution: 10 mg/mL

ASSAY

PROCEDURE

Sample solution: Dissolve 1000 mg of Ropivacaine Hydrochloride in 10 mL of water and 40 mL of alcohol. Add 1.0 mL of 1 N hydrochloric acid.

Analysis: Titrate with 1 N sodium hydroxide VS. Two equivalence points are obtained; the difference in titrant volume corresponds to the amount of ropivacaine hydrochloride (see [Titrimetry \(541\)](#)). Each mL of 1 N sodium hydroxide is equivalent to 310.9 mg of anhydrous ropivacaine hydrochloride ($C_{17}H_{26}N_2O \cdot HCl$).

Acceptance criteria: 98.5%–101.0% on the anhydrous basis

IMPURITIES

ORGANIC IMPURITIES

PROCEDURE 1

Buffer solution: Combine 1.3 mL of monobasic sodium phosphate solution (138 g/L) and 32.5 mL of disodium hydrogen phosphate dihydrate solution (89 g/L), and dilute with water to 1 L. The pH of this solution is 8.0. Make adjustments if necessary.

Mobile phase: Acetonitrile and Buffer solution (1:1)

System suitability solution: 10 µg/mL of each of [USP Ropivacaine Hydrochloride RS](#) and [USP Bupivacaine Hydrochloride RS](#) in Mobile phase

Sample solution 1: 2.75 mg/mL of Ropivacaine Hydrochloride in Mobile phase

Sample solution 2: 2.75 µg/mL of Ropivacaine Hydrochloride from Sample solution 1 diluted with Mobile phase

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 240 nm

Column: 3.9-mm × 15-cm; 4-μm packing L1

Flow rate: 1 mL/min

Injection volume: 20 μL

System suitability

[NOTE—Check the stability of the baseline by injecting *Mobile phase*. Run the chromatogram for at least 15 min.]

Samples: *System suitability solution* and *Sample solution 2*

[NOTE—The relative retention times for ropivacaine and bupivacaine are about 1.0 and 1.6, respectively.]

Suitability requirements

Resolution: NLT 6 between ropivacaine and bupivacaine, *System suitability solution*

Signal-to-noise ratio: NLT 10 for ropivacaine, *Sample solution 2*

Analysis

Samples: *System suitability solution* and *Sample solution 1*

Calculate the percentage of each impurity in the portion of Ropivacaine Hydrochloride taken:

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

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

r_T = sum of all the peak responses from the *Sample solution*

Acceptance criteria

Bupivacaine: NMT 0.2%

Any other individual impurity: Less than 0.1%

Total impurities: NMT 0.5%

• PROCEDURE 2: LIMIT OF ROPIVACAINE RELATED COMPOUND A

Buffer solution, Mobile phase, and Chromatographic system: Prepare as directed in *Procedure 1*.

Standard solution: 0.13 μg/mL of [USP Ropivacaine Related Compound A RS](#) in *Mobile phase*

Sample solution: 10 mg/mL of Ropivacaine Hydrochloride in *Mobile phase*

System suitability

Sample: *Standard solution*

Suitability requirements

Signal-to-noise ratio: NLT 10 for ropivacaine related compound A

Analysis

Samples: *Standard solution* and *Sample solution*

Acceptance criteria: The response for any peak corresponding to ropivacaine related compound A (2,6-dimethylaniline) in the *Sample solution* is not greater than the response of the major peak in the *Standard solution* (NMT 10 ppm).

• PROCEDURE 3: ENANTIOMERIC PURITY

Background electrolyte solution: 9.31–10.29 mg/mL of phosphoric acid in water. The pH is between 2.9 and 3.1. If necessary, adjust the pH with triethanolamine to 2.9–3.1.

Run buffer: 13.3 mg/mL of heptakis-(2,6-di-O-methyl)-β-cyclodextrin in *Background electrolyte solution*. [NOTE—This solution is freshly prepared and passed through a 0.45-μm filter.]

System suitability solution: 15 μg/mL of each [USP Ropivacaine Hydrochloride RS](#) and [USP Ropivacaine Related Compound B RS](#) in water

Sample solution 1: 2 mg/mL of Ropivacaine Hydrochloride in water

Sample solution 2: 0.01 mg/mL of ropivacaine hydrochloride from *Sample solution 1* diluted with water

Capillary rinsing procedure: Use separate *Run buffer* vials for capillary rinse and sample analysis. Rinse the capillary with water for 1 min, with 0.1 N sodium hydroxide for 10 min, and with water for 3 min. If a new or dry capillary is being used, increase the sodium hydroxide rinse time to 30 min. Rinse the capillary between injections as follows: water for 1 min, 0.1 N sodium hydroxide for 4 min, and water for 1 min, then *Run buffer* for 4 min. Rinse times are based on a rinse pressure of 1 bar.

Capillary electrophoresis system

Detector: UV 206 nm

Column: 50-μm × 72-cm fused silica

Column temperature: 30°

Applied voltage: 375 V/cm