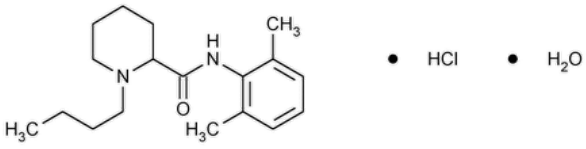
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-790CA6D8-A3E0-46CF-BE10-11B03B7EC29F_4_en-US
DOI: https://doi.org/10.31003/USPNF_M10490_04_01
DOI Ref: 59flf

Bupivacaine Hydrochloride



• HCl • H_2O

$C_{18}H_{28}N_2O \cdot HCl \cdot H_2O$ 342.90

2-Piperidinecarboxamide, 1-butyl-*N*-(2,6-dimethylphenyl)-, monohydrochloride, monohydrate, (±)-.

(±)-1-Butyl-2',6'-pipecoloxylidide monohydrochloride, monohydrate CAS RN®: 73360-54-0; UNII: 7TQO7W3VT8.

Anhydrous 324.90 CAS RN®: 18010-40-7; UNII: AKA908P8J1.

» Bupivacaine Hydrochloride contains not less than 98.5 percent and not more than 101.5 percent of $C_{18}H_{28}N_2O \cdot HCl$, calculated on the anhydrous basis.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—

USP Bupivacaine Hydrochloride RS

Identification—

Change to read:

A: ▲*Spectroscopic Identification Tests* ⟨197⟩, *Infrared Spectroscopy: 197S*▲ (CN 1-May-2020) —

Solution—Dissolve about 230 mg in 15 mL of water in a separator, add 1 mL of 6 N ammonium hydroxide, and extract with three 30-mL portions of chloroform. Evaporate the chloroform at room temperature with the aid of a stream of nitrogen, and dry the residue in vacuum. Add 2 mL of chloroform to the residue, and dissolve.

Change to read:

B: ▲*Spectroscopic Identification Tests* ⟨197⟩, *Ultraviolet-Visible Spectroscopy: 197U*▲ (CN 1-May-2020) —

Solution: 500 µg per mL.

Medium: 0.1 N hydrochloric acid.

Absorptivities at 271 nm, calculated on the anhydrous basis, do not differ by more than 3.0%.

C: Dissolve about 50 mg in 10 mL of water in a small separator, render alkaline with 6 N ammonium hydroxide, and extract with 10 mL of ether: the aqueous layer meets the requirements of the tests for *Chloride* ⟨191⟩.

pH ⟨791⟩**:** between 4.5 and 6.0, in a solution (1 in 100).

Water Determination, *Method I* ⟨921⟩**:** between 4.0% and 6.0%.

Residue on ignition ⟨281⟩**:** not more than 0.1%.

Limit of residual solvents—

Alcohol standard solution—Pipet 2 mL of dehydrated alcohol into a 100-mL volumetric flask, dilute with water to volume, and mix. Transfer 2.0 mL of this solution to a 50-mL volumetric flask, dilute with water to volume, and mix. The resulting solution contains 0.08% of alcohol.

Isopropyl alcohol standard solution—Pipet 2 mL of isopropyl alcohol into a 1000-mL volumetric flask, dilute with water to volume, and mix. Transfer 2.0 mL of this solution to a 100-mL volumetric flask, dilute with water to volume, and mix. The resulting solution contains 0.004% of isopropyl alcohol.

Test solution—Transfer 1.0 g of Bupivacaine Hydrochloride, accurately weighed, to a 25-mL volumetric flask, dilute with water to volume, and mix.

Chromatographic system—Under typical conditions, the instrument is equipped with a flame-ionization detector and a 4-mm × 2-m column that contains packing S3. The carrier gas is nitrogen, flowing at a rate of about 40 mL per minute. The column temperature is maintained at about 175°, the injection port temperature is maintained at about 200°, and the detector temperature is maintained at about 280°.

Procedure—Inject equal volumes (about 5 µL) of the *Test solution,* the *Alcohol standard solution,* and the *Isopropyl alcohol standard solution* successively into the gas chromatograph. Measure the responses of the alcohol peak and the isopropyl alcohol peak in each chromatogram. Determine the percentage of alcohol taken by the formula:

$$2(r_U/r_S)$$

and determine the percentage of isopropyl alcohol taken by the formula:

$$0.1(r_U/r_S)$$

in which r_U and r_S are the responses of the respective analytes in the *Test solution* and of the corresponding analytes in the *Alcohol standard solution* and the *Isopropyl alcohol standard solution,* respectively. The sum of the content of alcohol and the content of isopropyl alcohol does not exceed 2%.

Chromatographic purity—

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture.

Solvent: a mixture of chloroform and isopropylamine (99:1).

Test solution—Dissolve a suitable quantity of Bupivacaine Hydrochloride in *Solvent* to obtain a solution containing 20.0 mg per mL.

Standard solution—Dissolve a suitable quantity of USP Bupivacaine Hydrochloride RS, accurately weighed, in *Solvent* to obtain a solution containing 20.0 mg per mL.

Diluted standard solution—Quantitatively dilute a portion of the *Standard solution* in *Solvent* to obtain a solution having a concentration of 100 µg per mL.

Developing solvent system: a mixture of hexanes and isopropylamine (97:3).

Procedure—Apply separate 10-µL portions of the *Test Solution,* the *Standard solution,* and the *Diluted standard solution* on the starting line of suitable thin-layer chromatographic plate as directed for *Thin-Layer Chromatography* under *Chromatography* ⟨621⟩. Develop the chromatogram in a suitable chamber until the solvent has moved about three-fourths of the length of the plate. Remove the plate from the chamber, mark the solvent front, and dry it in warm air. Place the plate in a closed chamber with a dish containing 1 g of iodine in a shallow layer, and allow to remain for about 5 minutes. Remove the plate from the chamber, spray it with 7 N sulfuric acid, and examine the chromatogram: the R_F value of the principal spot from the *Test solution* corresponds to that of the *Standard solution,* and the estimated size and intensity of any other spot obtained from the *Test solution* does not exceed that of the principal spot obtained from the *Diluted standard solution* (0.5%); and the total of the estimated sizes and intensities of all of the other spots obtained from the *Test solution* does not exceed four times that of the principal spot obtained from the *Diluted standard solution* (2.0%).

Assay—Transfer about 600 mg of Bupivacaine Hydrochloride, accurately weighed, to a 250-mL conical flask, and dissolve in 20 mL of glacial acetic acid. Add 10 mL of mercuric acetate TS and 3 drops of crystal violet TS, and titrate with 0.1 N perchloric acid VS to a green endpoint. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 32.49 mg of $C_{18}H_{28}N_2O \cdot HCl$.

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 41(3)

Current DocID: GUID-790CA6D8-A3E0-46CF-BE10-11B03B7EC29F_4_en-US
DOI: https://doi.org/10.31003/USPNF_M10490_04_01
DOI ref: 59flf