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Ropivacaine Hydrochloride Injection

» Ropivacaine Hydrochloride Injection is a sterile solution of Ropivacaine Hydrochloride in Water for Injection. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of ropivacaine hydrochloride ($C_{17}H_{26}N_2O \cdot HCl$).

Packaging and storage—Preserve in single-dose or multiple-dose containers, preferably of Type 1 glass or of suitable plastic.

Change to read:

USP Reference standards ⟨11⟩—

USP Ropivacaine Hydrochloride RS

USP Ropivacaine Related Compound A RS

2,6-Dimethylaniline hydrochloride.

▲$C_8H_{11}N \cdot HCl$▲ (ERR 1-Jun-2020) 157.64 ▲▲ (ERR 1-Jun-2020)

USP Ropivacaine Related Compound B RS

(*R*)-Ropivacaine hydrochloride monohydrate; (*R*)-(+)-1-propylpiperidine-2-carboxylic acid (2,6-dimethylphenyl)-amide hydrochloride monohydrate; ▲(*R*)-*N*-(2,6-Dimethylphenyl)-1-propylpiperidine-2-carboxamide hydrochloride monohydrate.▲ (ERR 1-Jun-2020)

$C_{17}H_{26}N_2O$▲$\cdot HCl \cdot H_2O$ 328.88▲ (ERR 1-Jun-2020)

Identification—

A: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

B: The retention time of the major peak in the chromatogram of the *Test solution* corresponds to that in the chromatogram of the *System suitability solution,* as obtained in the test for *Enantiomeric purity*.

Bacterial Endotoxins Test ⟨85⟩—It contains not more than 60 USP Endotoxin Units per g of ropivacaine hydrochloride.

Particulate Matter in Injections ⟨788⟩**:** meets the requirements for injections.

Sterility Tests ⟨71⟩**:** It meets the requirements when tested as directed for *Membrane Filtration* under *Test for Sterility of the Product to be Examined*.

pH ⟨791⟩**:** between 4.0 and 6.0.

Limit of 2,6-dimethylaniline (ropivacaine related compound A, base)—

pH 8.0 Buffer solution and *Mobile phase*—Prepare as directed in the *Assay*.

Standard solution—Prepare as directed for *Standard preparation* in the *Assay*.

Test solution—Dilute accurately the Injection with *Mobile phase* to obtain a concentration of 2.0 mg per mL.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 240-nm detector and a 3.9-mm × 15-cm column that contains 5-µm packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between ropivacaine related compound A and ropivacaine is not less than 5; and the signal-to-noise ratio for ropivacaine related compound A is not less than 10.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. The peak response of ropivacaine related compound A obtained from the *Test solution* is not greater than the corresponding response obtained from the *Standard solution* (not more than 0.01% of ropivacaine related compound A base is found).

Enantiomeric purity—

pH 7.2 Buffer solution—Transfer 7.5 mL of 1 M monobasic sodium phosphate solution and 28.5 mL of 0.5 M dibasic sodium phosphate dihydrate solution into a 1-L volumetric flask, and dilute with water to volume. Adjust the resulting solution to a pH of 7.2, if necessary.

Mobile phase—Transfer 35 mL of isopropyl alcohol into a 500-mL volumetric flask, dilute with *pH 7.2 Buffer solution* to volume, mix, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

System suitability solution—Dissolve suitable quantities of USP Ropivacaine Hydrochloride RS and USP Ropivacaine Related Compound B RS in water, and dilute quantitatively, and stepwise, with water to obtain a solution containing about 75 µg per mL and 0.75 µg per mL, respectively.

Test solution—Dilute the Injection with *Mobile phase* to a concentration of about 75 µg per mL.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 220-nm detector and a 4-mm × 10-cm column that contains packing L41. The flow rate is about 1 mL per minute. Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between ropivacaine related compound B (*R* enantiomer) and ropivacaine (*S* enantiomer) is not less than 1.5. [Note—For the purpose of identification, the relative retention times are about 0.75 for ropivacaine related compound B and 1.0 for ropivacaine.]

Procedure—Inject about 20 µL of the *Test solution* into the chromatograph, record the chromatogram, and measure the peak responses. Calculate the percentage of ropivacaine related compound B (*R* enantiomer) in the portion of Injection taken by the formula:

$$100(r_i/r_s)$$

in which r_i is the peak response of ropivacaine related compound B (*R* enantiomer); and r_s is the sum of the peak responses of ropivacaine (*S* enantiomer) and ropivacaine related compound B (*R* enantiomer) obtained from the *Test solution:* not more than 2.0% of ropivacaine related compound B (*R* enantiomer) is found.

Other requirements—It meets the requirements under *Injections and Implanted Drug Products ⟨1⟩*.

Assay—

pH 8.0 Buffer solution—Transfer 1.3 mL of 1 M monobasic sodium phosphate solution and 32.5 mL of 0.5 M dibasic sodium phosphate dihydrate solution to a 1-L volumetric flask. Dilute with water to volume, and mix. Adjust the resulting solution to a pH of 8.0, if necessary.

Mobile phase—Prepare a filtered and degassed mixture of acetonitrile and *pH 8.0 Buffer solution* (60:40). Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Standard preparation—Dissolve accurately weighed quantities of USP Ropivacaine Hydrochloride RS and USP Ropivacaine Related Compound A RS in *Mobile phase,* and dilute quantitatively, and stepwise, with *Mobile phase* to obtain a solution having known concentrations of about 0.25 mg per mL of USP Ropivacaine Hydrochloride RS and about 0.26 µg per mL of USP Ropivacaine Related Compound A RS.

Assay preparation—Dilute accurately the Injection with *Mobile phase* to obtain a concentration of about 0.25 mg per mL.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 240-nm detector and a 3.9-mm × 15-cm column that contains 5- or 10-µm packing L1. The flow rate is about 1.2 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections, calculated for the ropivacaine peak, is not more than 1.0%; and the resolution, *R,* between ropivacaine related compound A and ropivacaine is not less than 5.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of ropivacaine hydrochloride ($C_{17}H_{26}N_2O \cdot HCl$) in each mL of Injection taken by the formula:

$$CD(r_U/r_S)$$

in which *C* is the concentration, in mg per mL, of USP Ropivacaine Hydrochloride RS in the *Standard preparation; D* is the dilution factor, in mL, for the *Assay preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

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

Topic/Question	Contact	Expert Committee
ROPIVACAINE HYDROCHLORIDE INJECTION	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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