

Fentanyl Citrate and Ropivacaine Hydrochloride Compounded Injection

DEFINITION

Fentanyl Citrate and Ropivacaine Hydrochloride Compounded Injection contains NLT 90.0% and NMT 110.0% of the labeled amount of fentanyl ($C_{22}H_{28}N_2O$) and ropivacaine hydrochloride ($C_{17}H_{26}N_2O \cdot HCl$).

Prepare Fentanyl Citrate and Ropivacaine Hydrochloride Compounded Injection containing 2 µg/mL of fentanyl and 1 mg/mL of ropivacaine hydrochloride as follows (see [Pharmaceutical Compounding—Nonsterile Preparations \(795\)](#)).

Fentanyl (as fentanyl citrate injection ^a), equivalent to	200 µg of fentanyl
Ropivacaine Hydrochloride (as ropivacaine hydrochloride injection ^b), equivalent to	100 mg of ropivacaine hydrochloride
Sodium Chloride for Injection (0.9%), a sufficient quantity to make	100 mL

- ^a Fentanyl Citrate 50-µg/mL injection, Hospira, Lake Forest, IL.
^b Ropivacaine Hydrochloride 0.5% (5 mg/mL) injection, Fresenius Kabi, Lake Zurich, IL.

Aseptically withdraw and combine 4 mL of the *Fentanyl Citrate injection* (50 µg/mL) (equivalent to 200 µg of fentanyl) and 20 mL of *Ropivacaine Hydrochloride injection* (5 mg/mL) (equivalent to 100 mg of ropivacaine hydrochloride) into an appropriate sterile container. Bring the preparation to a final volume of 100 mL with *Sodium Chloride for Injection (0.9%)*. Pass through a sterile filter of 0.22-µm pore size.

[NOTE—Do not use a cellulose ester filter membrane for sterilization due to potential for adsorption.]

ASSAY

• **PROCEDURE**

Solution A: Add 2.72 g of dibasic potassium phosphate to 800 mL of water. Adjust with phosphoric acid to a pH of 5.8. Add 200 mL of methanol and mix well.
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Methanol (%)	Solution A (%)
0.0	20	80
3.0	20	80
28.0	50	50
28.5	55	45
34.0	55	45
34.5	20	80
40	20	80

Standard solution: 2 µg/mL of fentanyl and 0.075 mg/mL of ropivacaine hydrochloride prepared from [USP Fentanyl Citrate RS](#) and [USP Ropivacaine Hydrochloride RS](#) in water
Ropivacaine hydrochloride sample solution: Transfer 0.75 mL of Injection into a 10-mL volumetric flask, and dilute with water to volume.
Fentanyl sample solution: 2 µg/mL of fentanyl from Injection

Chromatographic system(See [Chromatography \(621\), System Suitability](#).)**Mode:** LC**Detector:** UV 210 nm**Column:** 4.6-mm × 10-cm; 2.6-μm packing L1**Column temperature:** 40°**Flow rate:** 0.8 mL/min**Injection volume:** 20 μL**System suitability****Sample:** *Standard solution*

[NOTE—The retention times for ropivacaine hydrochloride and fentanyl are about 14.4 and 24.6 min, respectively.]

Suitability requirements**Tailing factor:** NMT 2.0 for both fentanyl and ropivacaine hydrochloride**Relative standard deviation:** NMT 2.0% for both fentanyl and ropivacaine hydrochloride from replicate injections**Analysis****Samples:** *Standard solution, Ropivacaine hydrochloride sample solution, and Fentanyl sample solution*Calculate the percentage of the labeled amount of fentanyl ($C_{22}H_{28}N_2O$) and ropivacaine hydrochloride ($C_{17}H_{26}N_2O \cdot HCl$) in the portion of Injection taken:

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

 r_U = peak response of fentanyl or ropivacaine hydrochloride from the relevant *Sample solution* r_S = peak response of fentanyl or ropivacaine hydrochloride from the *Standard solution* C_S = concentration of fentanyl or ropivacaine hydrochloride in the *Standard solution* (μg/mL or mg/mL, respectively) C_U = nominal concentration of fentanyl or ropivacaine hydrochloride in the relevant *Sample solution* (μg/mL or mg/mL, respectively)**Acceptance criteria:** 90.0%–110.0%• **ENANTIOMERIC PURITY****Mobile phase:** Add 0.418 g of monobasic sodium phosphate and 0.941 g of dibasic sodium phosphate to 465 mL of water. Adjust with sodium hydroxide to a pH of 7.2 and add 35 mL of isopropanol. Mix well.**System suitability solution:** Dissolve suitable quantities of [USP Ropivacaine Hydrochloride RS](#) and [USP Ropivacaine Related Compound B RS](#) in water. Dilute quantitatively, and stepwise, with water to obtain a solution containing about 75 μg/mL and 0.75 μg/mL, respectively.**Sample solution:** Transfer 0.75 mL of Injection into a 10-mL volumetric flask, and dilute with water to volume.**Chromatographic system**(See [Chromatography \(621\), System Suitability](#).)**Mode:** LC**Detector:** UV 220 nm**Column:** 4-mm × 10-cm; packing L41**Column temperature:** 25°**Flow rate:** 1.0 mL/min**Injection volume:** 20 μL**System suitability****Sample:** *System suitability solution*

[NOTE—The relative retention times for ropivacaine related compound B and ropivacaine hydrochloride are about 0.75 and 1.0, respectively.]

Suitability requirement**Resolution:** NLT 1.5 between ropivacaine related compound B (*R*-enantiomer) and ropivacaine (*S*-enantiomer)**Analysis****Sample:** *Sample solution*Calculate the percentage of ropivacaine related compound B (*R*-enantiomer) in the portion of Injection taken:

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

 r_U = peak response of ropivacaine related compound B (*R*-enantiomer) r_T = sum of the peak responses of ropivacaine (*S*-enantiomer) and ropivacaine related compound B (*R*-enantiomer)**Acceptance criteria:** NMT 2.0%**SPECIFIC TESTS****Change to read:**

- **pH (791):** ▲4.0–6.0▲ (USP 1-May-2024)