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Fentanyl Citrate and Bupivacaine Hydrochloride Compounded Injection

DEFINITION

Fentanyl Citrate and Bupivacaine Hydrochloride Compounded Injection contains NLT 90.0% and NMT 110.0% of the labeled amount of fentanyl ($C_{22}H_{28}N_2O$) and bupivacaine hydrochloride ($C_{18}H_{28}N_2O \cdot HCl$). It contains no bacteriostat or other preservative.

Prepare Fentanyl Citrate and Bupivacaine Hydrochloride Compounded Injection containing 2000 mcg/mL of fentanyl and 10 mg/mL of bupivacaine hydrochloride as follows (see *Pharmaceutical Compounding—Sterile Preparations* ⟨797⟩).

Fentanyl (as fentanyl citrate)	200 mg (314.6 mg)
Bupivacaine Hydrochloride	1000 mg
Sodium Chloride	695.5 mg
Sterile Water for Injection, a sufficient quantity to make	100 mL

Dissolve *Fentanyl Citrate*, *Bupivacaine Hydrochloride*, and *Sodium Chloride* in *Sterile Water for Injection*. Pass the solution through a suitable sterile filter of 0.22-µm pore size into appropriate sterile container(s).

[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 mcg/mL of fentanyl and 0.075 mg/mL of bupivacaine hydrochloride prepared from USP Fentanyl Citrate RS and USP Bupivacaine Hydrochloride RS in water

Bupivacaine hydrochloride sample solution: Transfer 0.75 mL of Injection into a 100-mL volumetric flask, and dilute with water to volume.

Fentanyl sample solution: Transfer 0.1 mL of Injection into a 100-mL volumetric flask, and dilute with water to volume.

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 bupivacaine hydrochloride and fentanyl are about 21.5 and 24.6 min, respectively.]

Suitability requirements

Tailing factor: NMT 2.0 for both fentanyl and bupivacaine hydrochloride

Relative standard deviation: NMT 2.0% for both fentanyl and bupivacaine hydrochloride from replicate injections

Analysis

Samples: *Standard solution* and sample solution

Calculate the percentage of the labeled amount of fentanyl ($C_{22}H_{28}N_2O$) and bupivacaine hydrochloride ($C_{18}H_{28}N_2O \cdot HCl$) 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 bupivacaine hydrochloride from the sample solution

r_S = peak response of fentanyl or bupivacaine hydrochloride from the *Standard solution*

C_S = concentration of fentanyl or bupivacaine hydrochloride in the *Standard solution* (mcg/mL or mg/mL, respectively)

C_U = nominal concentration of fentanyl or bupivacaine hydrochloride in the sample solution (mcg/mL or mg/mL, respectively)

Acceptance criteria: 90.0%–110.0%

SPECIFIC TESTS

• **pH** ⟨791⟩**:** 3.1–4.1

• **STERILITY TESTS** ⟨71⟩, *Test for Sterility of the Product to Be Examined, Membrane Filtration***:** Meets the requirements

• **BACTERIAL ENDOTOXINS TEST** ⟨85⟩**:** It contains NMT 50.0 USP Endotoxin Units/mg of fentanyl and NMT 2.5 USP Endotoxin Units/mg of bupivacaine hydrochloride.

• **PARTICULATE MATTER IN INJECTIONS** ⟨788⟩**:** Meets the requirements

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Package in a light-resistant, single-dose container. Store at controlled room temperature or in a refrigerator.

Change to read:

• **BEYOND-USE DATE:** ▲In the absence of passing a sterility and endotoxin test, the beyond-use dates in *Pharmaceutical Compounding—Sterile Preparations* ⟨797⟩ apply. After successful completion of sterility and endotoxin testing, NMT 90 days after the date on which it was compounded when stored at controlled room temperature or in a refrigerator.▲ (CN 1-May-2020)

• **LABELING:** The label bears a warning that this is a very high-strength injection. [NOTE—This is a high-strength injection.]Label it to indicate that it is for use in a single patient only, and to state the *Beyond-Use Date*.

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Bupivacaine Hydrochloride RS

USP Fentanyl Citrate RS

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

Topic/Question	Contact	Expert Committee
FENTANYL CITRATE AND BUPIVACAINE HYDROCHLORIDE COMPOUNDED INJECTION	Brian Serumaga Science Program Manager	CMP2020 Compounding 2020

Chromatographic Database Information: Chromatographic Database

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