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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 | <a href="#">Brian Serumaga</a><br>Science Program Manager | CMP2020 Compounding 2020 |

**Chromatographic Database Information:** [Chromatographic Database](#)

#### Most Recently Appeared In:

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