Morphine Sulfate Compounded Injection

DEFINITION

Morphine Sulfate Compounded Injection contains NLT 90.0% and NMT 110.0% of the labeled amount of morphine sulfate pentahydrate [$(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O$].

Prepare Morphine Sulfate Compounded Injection, 10 or 50 mg/mL, as follows (see *Pharmaceutical Compounding—Sterile Preparations* ⟨797⟩).

10-mg/mL Morphine Sulfate Compounded Injection

Morphine sulfate pentahydrate[a]	1 g
Sodium Chloride	760 mg
Sterile Water for Injection, a sufficient quantity to make	100 mL

[a] Morphine Sulfate, *USP*, is morphine sulfate pentahydrate; therefore no additional calculation is needed to account for the waters of hydration.

50-mg/mL Morphine Sulfate Compounded Injection

Morphine sulfate pentahydrate[a]	5 g
Sodium Chloride	450 mg
Sterile Water for Injection, a sufficient quantity to make	100 mL

[a] Morphine Sulfate, *USP*, is morphine sulfate pentahydrate; therefore no additional calculation is needed to account for the waters of hydration.

Dissolve the *Morphine sulfate pentahydrate* and *Sodium Chloride* in *Sterile Water for Injection* in a suitable calibrated container. Add sufficient *Sterile Water for Injection* to bring to final volume and mix well. Pass through a sterile filter of 0.22-µm pore size into sterile container(s).

ASSAY

Change to read:

- **PROCEDURE**

Solution A: Dissolve 5.44 g of dibasic potassium phosphate in 800 mL of water and add 200 mL of methanol.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Methanol (%)	Solution A (%)
0.0	0	100
3.0	▲0	100▲ (IRA 1-Sep-2019)
8.0	45	55
13.0	45	55
13.1	0	100
20.0	0	100

Standard solution: 1 mg/mL of morphine sulfate pentahydrate prepared from USP Morphine Sulfate RS in water

Sample solution: Transfer 0.4 mL of the 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 × ▲15-cm▲ (IRA 1-Sep-2019); 5-µm packing L1
Flow rate: 1.0 mL/min
Injection volume: 15 µL

System suitability
Sample: *Standard solution*
[NOTE—The retention time for morphine sulfate is about 10.5 min.]
Suitability requirements
Tailing factor: NMT 2.0
Relative standard deviation: NMT 2.0% for replicate injections

Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of morphine sulfate pentahydrate [$(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O$] in the portion of Injection taken:

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

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Morphine Sulfate RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of morphine sulfate pentahydrate in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

SPECIFIC TESTS

- **pH** ⟨791⟩**:** 2.5–6.5
- **STERILITY TESTS** ⟨71⟩**,** *Test for Sterility of the Product to Be Examined, Membrane Filtration***:** Meets the requirements

Change to read:

- **BACTERIAL ENDOTOXINS TEST** ⟨85⟩**:** ▲It contains NMT 17.0 USP Endotoxin Units/mg of morphine sulfate. If labeled for intrathecal use, it contains NMT 14.29 USP Endotoxin Units/mg of morphine sulfate.▲ (IRA 1-Sep-2019)
- **PARTICULATE MATTER IN INJECTIONS** ⟨788⟩**:** It meets the requirements.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Package in sterile syringes for single-use in one patient only, protected from light. Store at controlled room temperature.
- **BEYOND-USE DATE:** In the absence of passing a sterility and endotoxin test, the storage conditions for *High-Risk Level CSPs* apply (see *Pharmaceutical Compounding—Sterile Preparations* ⟨797⟩*, CSP Microbial Contamination Risk Levels, High-Risk Level CSPs*). 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.

Change to read:

- **LABELING:** Label it to indicate that it is for use in a single patient only. ▲Label it to indicate that it is preservative-free.▲ (IRA 1-Sep-2019) Label it to state the *Beyond-Use Date*.
- **USP REFERENCE STANDARDS** ⟨11⟩
USP Morphine Sulfate RS