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 \([(C_{17}H_{18}NO_3)_2 \cdot H_2SO_4 \cdot SH_2O_5]\).

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**

<table>
<thead>
<tr>
<th>Component</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium sulfate pentahydrate*</td>
<td>1 g</td>
</tr>
<tr>
<td>Sodium Chloride</td>
<td>760 mg</td>
</tr>
<tr>
<td>Sterile Water for Injection, a sufficient quantity to make</td>
<td>100 mL</td>
</tr>
</tbody>
</table>

*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**

<table>
<thead>
<tr>
<th>Component</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium sulfate pentahydrate*</td>
<td>5 g</td>
</tr>
<tr>
<td>Sodium Chloride</td>
<td>450 mg</td>
</tr>
<tr>
<td>Sterile Water for Injection, a sufficient quantity to make</td>
<td>100 mL</td>
</tr>
</tbody>
</table>

*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>
<thead>
<tr>
<th>Time (min)</th>
<th>Methanol (%)</th>
<th>Solution A (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>3.0</td>
<td>0</td>
<td>100 [IRA 1-Sep-2019]</td>
</tr>
<tr>
<td>8.0</td>
<td>45</td>
<td>55</td>
</tr>
<tr>
<td>13.0</td>
<td>45</td>
<td>55</td>
</tr>
<tr>
<td>13.1</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>20.0</td>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>

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 \([(C_{17}H_{18}NO_3)_2 \cdot H_2SO_4 \cdot SH_2O_5]\) in the portion of Injection taken:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times 100
\]

- \(r_U\) = 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.\([\text{IRA 1-Sep-2019}]\)
- **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.\([\text{IRA 1-Sep-2019}]\) Label it to state the Beyond-Use Date.
- **USP Reference Standards (11):** USP Morphine Sulfate RS