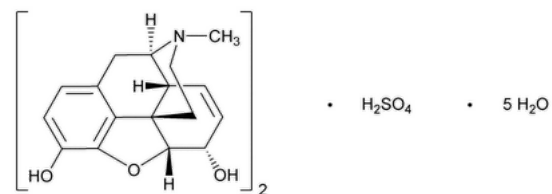


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Morphine Sulfate

Change to read:



$(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O$ 758.83

▲ $(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4$ ▲ (USP 1-Dec-2023) ▲668.76▲ (USP 1-Dec-2023)

Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5 α ,6 α)-, sulfate (2:1) (salt), pentahydrate;

7,8-Didehydro-4,5 α -epoxy-17-methylmorphinan-3,6 α -diol sulfate (2:1) (salt), pentahydrate CAS RN®: 6211-15-0; UNII: X3P646A2J0.

Anhydrous CAS RN®: 64-31-3; UNII: DY70C97N30.

DEFINITION

Morphine Sulfate contains NLT 98.0% and NMT 102.0% of morphine sulfate $(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4$, calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

- **A. SPECTROSCOPIC IDENTIFICATION TESTS** (197), *Infrared Spectroscopy*: 197K ▲ or 197A

Standard: Dry [USP Morphine Sulfate RS](#) at 145° for 1 h.

Sample: Dry Morphine Sulfate at 145° for 1 h.

Acceptance criteria: Meets the requirements▲ (USP 1-Dec-2023)

Change to read:

- **B.** ▲The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Dec-2023)

Delete the following:

- ▲• **C.**▲ (USP 1-Dec-2023)

Change to read:

- ▲**C.**▲ (USP 1-Dec-2023) [IDENTIFICATION TESTS—GENERAL](#) (191), *Chemical Identification Tests, Sulfate*

Sample solution: 20 mg/mL of Morphine Sulfate

Acceptance criteria: Meets the requirements

ASSAY

Change to read:

• PROCEDURE

Mobile phase: Dissolve 0.73 g of [sodium 1-heptanesulfonate](#) in 720 mL of [water](#), and add 280 mL of [methanol](#) and 10 mL of [glacial acetic acid](#).

System suitability solution: 0.24 mg/mL of [USP Morphine Sulfate RS](#) and 0.15 mg/mL of [phenol](#) in *Mobile phase*

Standard solution: 0.24 mg/mL of [USP Morphine Sulfate RS](#) in *Mobile phase*. Prepare a fresh solution daily.

Sample solution: 0.24 mg/mL of Morphine Sulfate in *Mobile phase*

Chromatographic system

(See [Chromatography](#) (621), *System Suitability*.)

Mode: LC

Detector: UV 284 nm

Column: 3.9-mm × 30-cm; ▲10- μ m▲ (USP 1-Dec-2023) packing [L1](#)

Flow rate: 1.5 mL/min

Injection volume: 25 μ L

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for phenol and morphine ▲▲ (USP 1-Dec-2023) are about 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between phenol and morphine ▲▲ (USP 1-Dec-2023), *System suitability solution*

Tailing factor: NMT 2.0, ▲ *Standard solution* ▲ (USP 1-Dec-2023)

Relative standard deviation: NMT ▲0.73%, ▲ (USP 1-Dec-2023) *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of morphine sulfate ($C_{17}H_{19}NO_3)_2 \cdot H_2SO_4$ in the portion of Morphine Sulfate taken:

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

r_U = peak response of morphine from the *Sample solution*

r_S = peak response of morphine from the *Standard solution*

C_S = concentration of anhydrous morphine sulfate in the *Standard solution* (mg/mL), as determined from the concentration of [USP Morphine Sulfate RS](#) corrected for moisture content by a titrimetric water determination

C_U = concentration of Morphine Sulfate in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#)

Sample: 500 mg of Morphine Sulfate

Acceptance criteria: NMT 0.1%

• CHLORIDE

Sample solution: 10 mg/mL of Morphine Sulfate in [water](#)

Analysis: To 10 mL of *Sample solution*, add 1 mL of 2 N [nitric acid](#) and 1 mL of [silver nitrate TS](#).

Acceptance criteria: No precipitate or turbidity is produced immediately.

• LIMIT OF FOREIGN ALKALOIDS

Sample solution: Dissolve 1.00 g of Morphine Sulfate in 10 mL of 1 N [sodium hydroxide](#) in a separator.

Analysis: Shake the *Sample solution*, with three successive portions of 15, 10, and 10 mL of [chloroform](#), passing the chloroform solutions through a small filter previously moistened with [chloroform](#). Shake the combined chloroform solutions with 5 mL of [water](#), separate the chloroform layer, and carefully evaporate on a steam bath to dryness. To the residue, add 10.0 mL of 0.020 N [sulfuric acid](#), and heat gently until dissolved. Cool, add 2 drops of [methyl red TS](#), and titrate the excess acid with 0.020 N [sodium hydroxide](#).

Acceptance criteria: NLT 7.5 mL is required (1.5%).

SPECIFIC TESTS

Change to read:

• [OPTICAL ROTATION \(781S\)](#), [Procedures](#), [Specific Rotation](#)

Sample solution: ▲▲ (USP 1-Dec-2023) 20 mg/mL ▲ of Morphine Sulfate ▲ (USP 1-Dec-2023) in [water](#)

Acceptance criteria: -107° to -110° ▲ (USP 1-Dec-2023)

• ACIDITY

Sample: 500 mg of Morphine Sulfate

Analysis: Dissolve the *Sample* in 15 mL of [water](#), add 1 drop of [methyl red TS](#), and titrate with 0.020 N [sodium hydroxide](#).

Acceptance criteria: NMT 0.50 mL is required to produce a yellow color.

• [WATER DETERMINATION \(921\)](#), [Method I](#): 10.4%–13.4%

Delete the following:

▲• AMMONIUM SALTS ▲ (USP 1-Dec-2023)

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers. Store up to 40° as permitted by the manufacturer.

• [USP REFERENCE STANDARDS \(11\)](#)

[USP Morphine Sulfate RS](#)