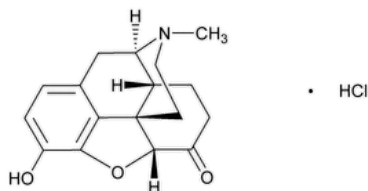


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Hydromorphone Hydrochloride



$C_{17}H_{19}NO_3 \cdot HCl$ 321.80
Morphinan-6-one, 4,5-epoxy-3-hydroxy-17-methyl-, hydrochloride, (5 α)-;
4,5 α -Epoxy-3-hydroxy-17-methylmorphinan-6-one hydrochloride CAS RN®: 71-68-1; UNII: L960UP2KRW.

DEFINITION

Hydromorphone Hydrochloride contains NLT 98.0% and NMT 102.0% of hydromorphone hydrochloride ($C_{17}H_{19}NO_3 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

Change to read:

- **A.** ▲ [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#): 197A or 197K▲ (CN 1-May-2020)
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
- **C.** [IDENTIFICATION TESTS—GENERAL \(191\)](#), [Chemical Identification Tests, Chloride](#)

Sample solution: 1 in 20
Acceptance criteria: Meets the requirements

ASSAY

- **PROCEDURE**
Solution A: 1.0 mg/mL of [sodium 1-heptanesulfonate monohydrate](#) in 1000 mL of [methanol](#) and [water](#) (1:9). Add 1.0 mL of [triethylamine](#) and adjust with [phosphoric acid](#) to a pH of 2.5 ± 0.1 .
Solution B: 1.0 mg/mL of [sodium 1-heptanesulfonate monohydrate](#) in 1000 mL of [methanol](#) and [water](#) (1:1). Add 1.0 mL of [triethylamine](#) and adjust with [phosphoric acid](#) to a pH of 2.5 ± 0.1 .
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	94	6
25	94	6
30	0	100
32	0	100
32.1	94	6

Time (min)	Solution A (%)	Solution B (%)
35	94	6

Diluent: [Phosphoric acid](#) and [water](#) (1:1000)

Standard solution: 0.4 mg/mL of [USP Hydromorphone Hydrochloride RS](#) in *Diluent*

Sample solution: 0.4 mg/mL of Hydromorphone Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 3.9-mm × 15-cm; 5-μm packing L1

Column temperature: 45°

Flow rate: 1.0 mL/min

Injection volume: 20 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of hydromorphone hydrochloride ($C_{17}H_{19}NO_3 \cdot HCl$) in the portion of Hydromorphone Hydrochloride taken:

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

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

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

C_S = concentration of [USP Hydromorphone Hydrochloride RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Hydromorphone Hydrochloride in the *Sample solution* (mg/mL)

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

IMPURITIES

- [RESIDUE ON IGNITION \(281\)](#): NMT 0.3%

[NOTE—On the basis of the synthetic route, perform either *Organic Impurities, Procedure 1* or *Organic Impurities, Procedure 2*. *Organic Impurities, Procedure 2* is recommended when hydromorphone aldol dimer and 7,8'-bishydromorphone may be present.]

- **ORGANIC IMPURITIES, PROCEDURE 1**

Solution A, Solution B, Diluent, and Chromatographic system: Proceed as directed in the Assay.

Mobile phase: See [Table 2](#).

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	94	6
25	94	6
40	20	80
70	20	80

