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Hydromorphone Hydrochloride Oral Solution

DEFINITION
Hydromorphone Hydrochloride Oral Solution contains NLT 90.0% and NMT 110.0% of the labeled amount of hydromorphone hydrochloride ($C_{17}H_{19}NO_3 \cdot HCl$). It may contain suitable preservatives.

IDENTIFICATION
• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
• **PROCEDURE**
Diluent: Phosphoric acid and water (1:1000)
Solution A: 1.0 mg/mL of sodium 1-heptanesulfonate monohydrate in methanol and water (1:9). To each liter of this solution 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 methanol and water (1:1). To each liter of this solution 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	85	15
24	5	95
25	85	15
30	85	15

The *Standard solution* and *Sample solution* should be kept in a cool place, protected from light.

Standard solution: 0.08 mg/mL of [USP Hydromorphone Hydrochloride RS](#) in *Diluent*
Sample solution: Nominally 0.08 mg/mL of hydromorphone hydrochloride obtained by diluting a suitable volume of Oral Solution in *Diluent*

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

Mode: LC
Detector: UV 220 nm
Column: 4.6-mm × 5-cm; 3.5-μm packing L1
Column temperature: 45°
Flow rate: 1 mL/min
Injection volume: 20 μL

System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 1.5 for the hydromorphone peak
Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of hydromorphone hydrochloride ($C_{17}H_{19}NO_3 \cdot HCl$) in the portion of Oral Solution 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 Hydromorphone Hydrochloride RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of hydromorphone hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

IMPURITIES

Change to read:

• ORGANIC IMPURITIES

Diluent, Solution A, and Solution B: Prepare 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
75	94	6
90	94	6

The *System suitability solution*, *Quantitation limit solution*, *Standard solution*, and *Sample solution* should be kept in a cool place, protected from light.

System suitability solution: 0.8 mg/mL of [USP Hydromorphone Hydrochloride RS](#) and 0.8 µg/mL of [USP Hydromorphone Related Compound A RS](#) in *Diluent*

Quantitation limit solution: 0.4 µg/mL of [USP Hydromorphone Hydrochloride RS](#) in *Diluent*

Standard solution: 4 µg/mL of [USP Hydromorphone Hydrochloride RS](#) in *Diluent*

Sample solution: Nominally 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 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution*, *Quantitation limit solution*, and *Standard solution*

Suitability requirements

Resolution: NLT 1.0 between the hydromorphone related compound A and hydromorphone peaks, *System suitability solution*

Signal-to-noise ratio: NLT 10:1, *Quantitation limit solution*

Tailing factor: NMT 1.5 for the hydromorphone peak, *Standard solution*