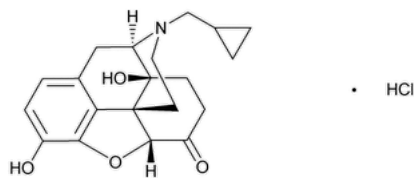


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Naltrexone Hydrochloride



$C_{20}H_{23}NO_4 \cdot HCl$ 377.86
Morphinan-6-one, 17-(cyclopropylmethyl)-4,5-epoxy-3,14- dihydroxy-, hydrochloride, (5 α);
17-(Cyclopropylmethyl)-4,5 α -epoxy-3,14-dihydroxy morphinan-6-one hydrochloride CAS RN®: 16676-29-2; UNII: Z6375YW9SF.
Free base
 $C_{20}H_{23}NO_4$ 341.41 CAS RN®: 16590-41-3; UNII: 5S6W795CQM.
Dihydrate
 $C_{20}H_{23}NO_4 \cdot HCl \cdot 2H_2O$ 413.89 CAS RN®: 850808-02-5; UNII: 5P80UKS30B.

DEFINITION

Naltrexone Hydrochloride contains NLT 98.0% and NMT 102.0% of naltrexone hydrochloride ($C_{20}H_{23}NO_4 \cdot HCl$), calculated on the anhydrous, solvent-free basis.

IDENTIFICATION

Change to read:

- **A.** ▲ **SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197A or 197K▲ (CN 1-May-2020)
Sample: Dissolve 150 mg of Naltrexone Hydrochloride in 25 mL of [water](#) in a small separator. Add a few drops of 6 N [ammonium hydroxide](#) slowly until no more white precipitate is formed. Extract with three 5-mL portions of [chloroform](#), and pass the extracts through a dry filter, collecting the filtrate in a small flask. Evaporate the filtrate on a steam bath to dryness, and dry the residue at 105° for 1 h.
Acceptance criteria: Meets the requirements
- **B.** The retention time of the naltrexone peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

• **PROCEDURE**

- Solution A:** Dissolve about 1.08 g of [sodium 1-octanesulfonate](#) and about 23.8 g of [sodium acetate](#) in 800 mL of [water](#). Add 1.0 mL of [triethylamine](#) and 200 mL of [methanol](#), and adjust with [glacial acetic acid](#) to a pH of 6.5 ± 0.1.
- Solution B:** Dissolve about 1.08 g of [sodium 1-octanesulfonate](#) and about 23.8 g of [sodium acetate](#) in 400 mL of water. Add 1.0 mL of [triethylamine](#) and 600 mL of [methanol](#), and adjust with [glacial acetic acid](#) to a pH of 6.5 ± 0.1.
- Mobile phase:** See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
35	0	100
36	100	0
53	100	0

Standard solution: 2.25 mg/mL of [USP Naltrexone RS](#) prepared as follows. Transfer an amount of [USP Naltrexone RS](#) to a suitable volumetric flask, add 15% of the final volume of methanol and 6% of the final volume of 0.1 N hydrochloric acid, and dissolve by swirling. Dilute with 0.1 M [phosphoric acid](#) to volume.

System suitability stock solution: 0.3 mg/mL of [USP Naltrexone Related Compound A RS](#) prepared as follows. Transfer a quantity of [USP Naltrexone Related Compound A RS](#) to a suitable volumetric flask, add 30% of the final volume of [methanol](#), and dissolve by swirling. Dilute with 0.1 M [phosphoric acid](#) to volume.

System suitability solution: 1.125 mg/mL of [USP Naltrexone RS](#) and 0.015 mg/mL of [USP Naltrexone Related Compound A RS](#) prepared as follows. Transfer suitable volumes of *System suitability stock solution* and *Standard solution* to an adequate volumetric flask, and dilute with 0.1 M [phosphoric acid](#) to volume.

Sample solution: 2.5 mg/mL of Naltrexone Hydrochloride in 0.1 M [phosphoric acid](#)

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 3.9-mm × 15-cm; 4-μm packing L1

Flow rate: 1 mL/min

Injection volume: 20 μL

System suitability

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

[NOTE—The relative retention times for naltrexone and naltrexone related compound A are 1.0 and 1.26, respectively.]

Suitability requirements

Resolution: NLT 2.0 between naltrexone and naltrexone related compound A, *System suitability solution*

Tailing factor: NMT 1.4, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of naltrexone hydrochloride ($C_{20}H_{23}NO_4 \cdot HCl$) in the portion of Naltrexone Hydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

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

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

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

M_{r1} = molecular weight of naltrexone hydrochloride, 377.86

M_{r2} = molecular weight of naltrexone, 341.41

Acceptance criteria: 98.0%–102.0% on the anhydrous, solvent-free basis

IMPURITIES

• **RESIDUE ON IGNITION (281):** NMT 0.1%

• **LIMIT OF TOTAL SOLVENTS:** The sum of water and total solvents (methanol and ethanol) is NMT 5.0% for the anhydrous form and NMT 11.0% for the dihydrate form.

• **ORGANIC IMPURITIES**

Solution A, Solution B, Mobile phase, Standard solution, System suitability stock solution, System suitability solution, Sample solution, and Chromatographic system: Proceed as directed in the Assay.

Sensitivity solution: 2.25 μg/mL of [USP Naltrexone RS](#) in 0.1 M [phosphoric acid](#) from *Standard solution*

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between naltrexone and naltrexone related compound A, *System suitability solution*

Tailing factor: NMT 1.4, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Naltrexone Hydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*