

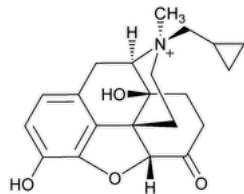
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Methylnaltrexone Bromide

Change to read:

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▲ (ERR 1-Mar-2024)

$C_{21}H_{26}BrNO_4$ 436.34

Morphinanium, 17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxy-17-methyl-6-oxo-, bromide, (5 α ,17*R*)-;
(17*R*)-17-(Cyclopropylmethyl)-4,5 α -epoxy-3,14-dihydroxy-17-methyl-6-oxomorphinanium bromide CAS RN[®]: 916055-92-0.

DEFINITION

Methylnaltrexone Bromide contains NLT 98.0% and NMT 102.0% of methylnaltrexone bromide ($C_{21}H_{26}BrNO_4$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

- **A.** [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#): 197A or 197K
- **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, Bromide](#): Meets the requirements of the silver nitrate precipitation test

ASSAY

• **PROCEDURE**

Protect solutions containing methylnaltrexone bromide from light.

Buffer: Dilute 3.0 mL of [heptafluorobutyric acid](#) with [water](#) to 1000 mL. Adjust with [ammonium hydroxide](#) to a pH of 2.4.

Solution A: *Buffer* and methanol (85:15)

Solution B: *Buffer*, methanol, and [tetrahydrofuran](#) (85:5:10)

Mobile phase: See [Table 1](#). Return to original conditions and re-equilibrate the system for about 15 min.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
15	30	70
50	30	70

Diluent: *Solution A*

Standard solution: 3.0 mg/mL of [USP Methylnaltrexone Bromide RS](#) in *Diluent*

Sample solution: 3.0 mg/mL of Methylnaltrexone Bromide in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 25-cm; 3- μ m packing [L1](#)

Column temperature: 50°

Flow rate: 1.0 mL/min

Injection volume: 50 μ L

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 methylnaltrexone bromide ($C_{21}H_{26}BrNO_4$) in the portion of Methylnaltrexone Bromide 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 Methylnaltrexone Bromide RS](#) in the *Standard solution* (mg/mL) C_U = concentration of Methylnaltrexone Bromide in the *Sample solution* (mg/mL)**Acceptance criteria:** 98.0%–102.0% on the anhydrous and solvent-free basis**IMPURITIES**• [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%• **ORGANIC IMPURITIES**

Protect solutions containing methylnaltrexone bromide from light.

Solution A, Solution B, Mobile phase, Diluent, Sample solution, and Chromatographic system: Proceed as directed in the Assay.**System suitability solution:** 3.0 mg/mL of [USP Methylnaltrexone Bromide RS](#) and 4.5 µg/mL of [USP Naltrexone RS](#) in *Diluent***Sensitivity solution:** 1.5 µg/mL of [USP Methylnaltrexone Bromide RS](#) in *Diluent***Standard solution:** 4.5 µg/mL of [USP Methylnaltrexone Bromide RS](#) in *Diluent***System suitability****Samples:** *System suitability solution, Sensitivity solution, and Standard solution***Suitability requirements****Resolution:** NLT 1.5 between methylnaltrexone bromide and naltrexone, *System suitability solution***Relative standard deviation:** NMT 5.0%, *Standard solution***Signal-to-noise ratio:** NLT 10, *Sensitivity solution***Analysis****Samples:** *Sample solution and Standard solution*

Calculate the percentage of each impurity in the portion of Methylnaltrexone Bromide taken:

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

 r_U = peak response of each impurity from the *Sample solution* r_S = peak response of methylnaltrexone from the *Standard solution* C_S = concentration of [USP Methylnaltrexone Bromide RS](#) in the *Standard solution* (mg/mL) C_U = concentration of Methylnaltrexone Bromide in the *Sample solution* (mg/mL)**Acceptance criteria:** See [Table 2](#). The reporting threshold is 0.05%.**Table 2**

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
S-Methylnaltrexone ^a	0.92	0.15
Methylnaltrexone	1.0	—
Naltrexone	1.15	0.15
N-Butenyl oxymorphone ^b	1.21	