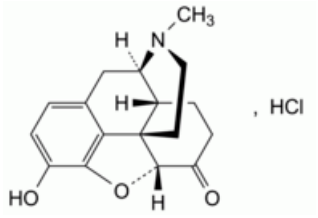
Edition: BP 2025 (Ph. Eur. 11.6 update)

# Hydromorphone Hydrochloride

General Notices

*(Ph. Eur. monograph 2099)*




$C_{17}H_{20}ClNO_3$ 321.8 *71-68-1*

**Action and use**

Opioid receptor agonist; analgesic.

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## DEFINITION

4,5α-Epoxy-3-hydroxy-17-methylmorphinan-6-one hydrochloride.

**Content**

99.0 per cent to 101.0 per cent (dried substance).

## CHARACTERS

**Appearance**

White or almost white, crystalline powder.

**Solubility**

Freely soluble in water, very slightly soluble in ethanol (96 per cent), practically insoluble in methylene chloride.

## IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24).

*Comparison* *hydromorphone hydrochloride CRS*.

B. It gives reaction (a) of chlorides (2.3.1).

## TESTS

### Solution S

Dissolve 1.250 g in *carbon dioxide-free water R* and dilute to 25.0 mL with the same solvent.

### Appearance of solution

Solution S is clear (2.2.1) and not more intensely coloured than reference solution $BY_5$ (2.2.2, *Method II*).

### Acidity or alkalinity

To 2 mL of solution S add 0.1 mL of *methyl red solution R*. The solution is not yellow. To 2 mL of solution S add 0.05 mL of *bromocresol green solution R*. The solution is not yellow.

### Specific optical rotation (2.2.7)

-136 to -140 (dried substance), determined on solution S.

### Related substances

Liquid chromatography (2.2.29).

*Test solution* Dissolve 0.100 g of the substance to be examined in *water R*, sonicating if necessary and dilute to 100.0 mL with the same solvent.

*Reference solution (a)* Dilute 1.0 mL of the test solution to 100.0 mL with *water R*. Dilute 1.0 mL of this solution to 10.0 mL with *water R*.

*Reference solution (b)* To 5 mL of the test solution add 5 mg of *naloxone hydrochloride dihydrate CRS* and dilute to 50 mL with *water R*.

*Column*:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: *base-deactivated end-capped octadecylsilyl silica gel for chromatography R* (5 µm).

*Mobile phase* Dissolve 18.29 g of *diethylamine R* and 2.88 g of *sodium laurilsulfate R* in *water R* and dilute to 1000 mL with the same solvent. Adjust 800 mL of this solution to pH 3.0 with *phosphoric acid R*. Add 100 mL of *acetonitrile R* and 100 mL of *methanol R*.

*Flow rate* 1 mL/min.

*Detection* Spectrophotometer at 284 nm.

*Injection* 20 µL.

*Run time* 4 times the retention time of hydromorphone.

*Relative retention* With reference to hydromorphone (retention time = about 9 min): impurity D = about 0.72; impurity B = about 0.77; impurity C = about 0.82; impurity A = about 3.2.

*System suitability* Reference solution (b):

— *resolution*: minimum 4.0 between the peaks due to hydromorphone and naloxone.

*Limits*:

— *impurity A*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 per cent);

— *impurities B, C, D*: for each impurity, not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);

— *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);

— *total*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent);

— *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

**Loss on drying** (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

**Sulfated ash** (*2.4.14*)

Maximum 0.1 per cent, determined on the residue obtained in the test for loss on drying.

## ASSAY

Dissolve 0.250 g in 50 mL of *ethanol (96 per cent) R* and add 5.0 mL of *0.01 M hydrochloric acid*. Carry out a potentiometric titration (*2.2.20*), using *0.1 M sodium hydroxide*. Read the volume added between the 2 points of inflexion.

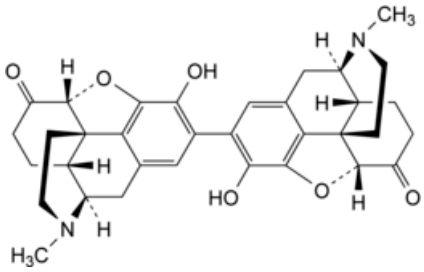
1 mL of *0.1 M sodium hydroxide* is equivalent to 32.18 mg of $C_{17}H_{20}ClNO_3$.

## STORAGE

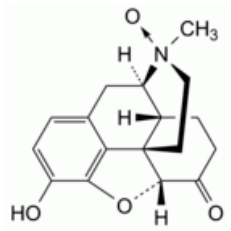
Protected from light.

## IMPURITIES

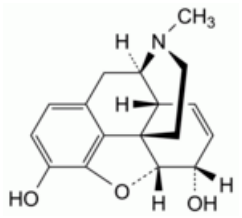
*Specified impurities* *A, B, C, D.*



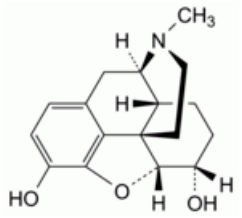
A. 4,5α:4′,5′α-diepoxy-3,3′-dihydroxy-17,17′-dimethyl-2,2′-bimorphinanyl-6,6′-dione (pseudohydromorphone),



B. 4,5α-epoxy-3-hydroxy-17-methylmorphinan-6-one 17-oxide (hydromorphone *N*-oxide),




C. 7,8-didehydro-4,5α-epoxy-17-methylmorphinan-3,6α-diol (morphine),




D. 4,5α-epoxy-17-methylmorphinan-3,6α-diol (dihydromorphine).

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