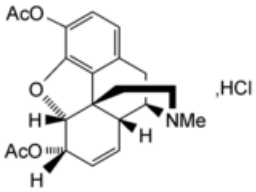
Edition: BP 2025 (Ph. Eur. 11.6 update)

Diamorphine Hydrochloride

General Notices



$C_{21}H_{23}NO_5$,HCl,H_2O 423.9 *1502-95-0*

Action and use

Opioid receptor agonist; analgesic.

Preparations

Bupivacaine and Diamorphine Injection

Diamorphine Tablets

Diamorphine Injection

DEFINITION

Diamorphine Hydrochloride is 4,5-epoxy-17-methylmorphinan-3,6-diyl diacetate hydrochloride monohydrate. It contains not less than 98.0% and not more than 102.0% of $C_{21}H_{23}NO_5$,HCl, calculated with reference to the dried substance.

CHARACTERISTICS

A white or almost white, crystalline powder.

Freely soluble in *water*; soluble in *ethanol (96%)*; practically insoluble in *ether*.

IDENTIFICATION

A. Dissolve a sufficient quantity in the minimum volume of *dichloromethane* and evaporate to dryness. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of diamorphine hydrochloride *(RS 093)*.
B. Yields reaction A characteristic of *chlorides*, Appendix VI.

TESTS

Acidity

Dissolve 0.2 g in 10 mL of *carbon dioxide-free water* and titrate with *0.02M sodium hydroxide VS* using *methyl red solution* as indicator. Not more than 0.2 mL of *0.02M sodium hydroxide VS* is required.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) 0.5% w/v of the substance being examined in *water*.
(2) Dilute 1 volume of solution (1) to 50 volumes with *water*.
(3) A freshly prepared solution containing 0.1% w/v of the substance being examined in 0.01M *sodium hydroxide*.
(4) Dilute 1 volume of solution (2) to 20 volumes with *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (12.5 cm × 4.6 mm) packed with *base-deactivated octylsilyl silica gel for chromatography*, (5 µm) (Lichrospher RP-select B is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 283 nm.
(f) Inject 20 µL of each solution.
(g) Allow the chromatography to proceed for twice the retention time of the peak due to diamorphine hydrochloride.

MOBILE PHASE

0.11 % w/v of *sodium octanesulfonate* in a mixture of 10 volumes of *glacial acetic acid*, 10 volumes of *methanol*, 115 volumes of *acetonitrile* and 365 volumes of *water*.

SYSTEM SUITABILITY

The test is not valid unless:

the chromatogram obtained with solution (3) exhibits two *secondary peaks* with retention times relative to the principal peak of about 0.23 (morphine) and 0.43 (6-*O*-acetyl-morphine);

in the chromatogram obtained with solution (3), the *resolution factor* between the peaks due to morphine and 6-*O*-acetyl-morphine is at least 2.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to 6-*O*-acetylmorphine is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (2%);

the sum of the areas of any other *secondary peaks* is not greater than 0.25 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

Loss on drying

When dried to constant weight at 105°, loses 3.0 to 4.5% of its weight. Use 1 g.

Sulfated ash

Not more than 0.1%, Appendix IX A.

ASSAY

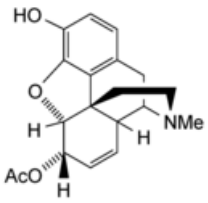
Dissolve 0.40 g in 50 mL of *ethanol (96%)* and add 5.0 mL of *0.01M hydrochloric acid VS*. Titrate with *0.1M sodium hydroxide VS* , determining the end point potentiometrically. Measure the volume of titrant required between the two points of inflection. Each mL of *0.1M sodium hydroxide VS* is equivalent to 40.59 mg of $C_{21}H_{23}NO_5$,HCl.

STORAGE

Diamorphine Hydrochloride should be protected from light.

IMPURITIES

The impurity limited by this monograph is:



A. 6-*O*-acetylmorphine.