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

Diamorphine Tablets

General Notices

Action and use

Opioid receptor agonist analgesic.

DEFINITION

Diamorphine Tablets contain Diamorphine Hydrochloride.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of diamorphine hydrochloride, $C_{21}H_{23}NO_5,HCl,H_2O$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the powdered tablets containing 10 mg of Diamorphine Hydrochloride with 10 mL of *dichloromethane*, filter 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)*.

TESTS

Dissolution

Comply with the requirements in the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of *0.1M hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

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

(1) After 15 minutes withdraw a sample of the medium and filter. Use the filtered medium, diluted with *water* if necessary, to produce a solution expected to contain 0.0011% w/v of Diamorphine Hydrochloride.
(2) 0.0011% w/v of *diamorphine hydrochloride BPCRS* in the dissolution medium.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Spherisorb ODS2 is suitable).

(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 30°.
(e) Use a detection wavelength of 260 nm.
(f) Inject 250 µL of each solution.

MOBILE PHASE

45 volumes of *acetonitrile* and 55 volumes of 0.01M *sodium heptanesulfonate*, containing 0.0075M N,N-*dimethyloctylamine*, which has been adjusted to pH 3.0 with *orthophosphoric acid*.

DETERMINATION OF CONTENT

Calculate the total content of $C_{21}H_{23}NO_5$,HCl,H_2O in the medium from the chromatograms obtained and using the declared content of $C_{21}H_{23}NO_5$,HCl,H_2O in *diamorphine hydrochloride BPCRS*.

LIMITS

The amount of diamorphine hydrochloride released is not less than 75% (Q) of the stated amount.

Related substances

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

(1) Disperse a quantity powdered tablets containing 80 mg of Diamorphine Hydrochloride in 10 mL of *water*.
(2) Dilute 1 volume of solution (1) to 100 volumes with *water*.
(3) Disperse a quantity of the powdered tablets to give a solution containing 0.1% w/v of Diamorphine Hydrochloride in 0.01M *sodium hydroxide*; the solution should be freshly prepared.
(4) Dilute 1 volume of solution (2) to 10 volumes with *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (12.5 cm × 4.6 mm) packed with *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 50 µL of each solution.
(g) For solution (1), allow the chromatography to proceed for twice the retention time of the peak due to diamorphine.

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*.

When the chromatograms are recorded under the prescribed conditions the retention time of diamorphine is about 20 minutes.

SYSTEM SUITABILITY

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). The test is not valid unless the *resolution* 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 twice the area of the principal peak in the chromatogram obtained with solution (2) (2%);

the area of any other *secondary peaks* is not greater than twice the area of the principal peak in the chromatogram obtained with solution (4) (0.2%);

the sum of the areas of any other *secondary peaks* is not greater than half 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%).

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Disperse a quantity of the powdered tablets containing 30 mg of Diamorphine Hydrochloride in *water*, dilute to 100 mL with *water*.
(2) 0.03% w/v of *diamorphine hydrochloride BPCRS* in *water*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used with an injection volume of 10 µL.

MOBILE PHASE

45 volumes of *acetonitrile* and 55 volumes of 0.01M *sodium heptanesulfonate*, containing 0.0075M N,N-*dimethyloctylamine*, which has been adjusted to pH 3.0 with *orthophosphoric acid*.

DETERMINATION OF CONTENT

Calculate the content of $C_{21}H_{23}NO_5,HCl,H_2O$ in the tablets using the declared content of $C_{21}H_{23}NO_5,HCl,H_2O$ in *diamorphine hydrochloride BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph those listed under Diamorphine Hydrochloride.