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

Pethidine Injection

General Notices

Action and use

Opioid receptor agonist; analgesic.

DEFINITION

Pethidine Injection is a sterile solution of Pethidine Hydrochloride in Water for Injections.

The injection complies with the requirements stated under Parenteral Preparations and with the following requirements.

PRODUCTION

The manufacturing process of Pethidine Hydrochloride, used in the formulation of Pethidine Injection, is validated to show that the content of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine is not more than 0.1 ppm.

Content of pethidine hydrochloride, $C_{15}H_{21}NO_2$,HCl

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. To a volume containing 50 mg of Pethidine Hydrochloride add sufficient 1M *sodium hydroxide* to make strongly alkaline to *litmus paper* and extract with two 10 mL quantities of *chloroform*. Wash the combined extracts with 5 mL of *water*, dry over *anhydrous sodium sulfate*, filter and evaporate the filtrate to dryness. Remove the last traces of chloroform by drying the residual oil at 60° at a pressure not exceeding 0.7 kPa. The *infrared absorption spectrum* of the oily residue, Appendix II A, is concordant with the *reference spectrum* of pethidine (*RS 266*).
B. Yields the reactions characteristic of *chlorides*, Appendix VI.

Related substances

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

(1) Dilute a volume of the injection containing 0.1 g of Pethidine Hydrochloride to 25 mL with a mixture of 20 volumes of *acetonitrile R1* and 80 volumes of *water*.
(2) Dilute 0.5 volumes of solution (1) to 100 volumes with a mixture of 20 volumes of *acetonitrile R1* and 80 volumes of *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.0 mm) packed with *spherical end-capped octadecylsilyl silica gel for chromatography* (5 µm) with a specific surface area of 340 m^2/g, a pore size of 10 nm and a carbon loading of 19% (Kromasil C18 is suitable).
(b) Use gradient 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 210 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A Mix equal volumes of a 4.2% w/v solution of *sodium perchlorate* and a 1.2% w/v solution of *orthophosphoric acid*. Adjust the pH to 2.0 with *triethylamine*.

Mobile phase B *acetonitrile R1*.

Time	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0–15	80 → 75	20 → 25
15–31	75 → 55	25 → 45
31–40	55	45
40–41	55 → 80	45 → 20
41–50	80	20

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the sum of the areas of any such peaks is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (1%).

Disregard any peak with an area less than 0.1 times the area of the peak in the chromatogram obtained with solution (2) (0.05%).

ASSAY

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

(1) Dilute the injection, if necessary, with sufficient *water* to produce a solution containing 0.1% w/v of Pethidine Hydrochloride and further dilute 3 volumes of the resulting solution to 25 volumes with the mobile phase.
(2) Dilute 3 volumes of a 0.10% w/v solution of *pethidine hydrochloride BPCRS* to 25 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Spherisorb ODS1 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 230 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

11 volumes of *acetonitrile* and 9 volumes of a mixture prepared in the following manner: dissolve 6.8 g of *potassium dihydrogen orthophosphate* in 1000 mL of *water*, add 10 mL *triethylamine*, mix well and adjust the solution to pH 7.0 with *orthophosphoric acid*.

SYSTEM SUITABILITY

The *column efficiency*, determined on the peak due to pethidine in the chromatogram obtained with solution (2), should be at least 8000 *theoretical plates* per metre.

DETERMINATION OF CONTENT

Calculate the content of $C_{15}H_{21}NO_2$,HCl in the injection using the declared content of $C_{15}H_{21}NO_2$,HCl in *pethidine hydrochloride BPCRS*.