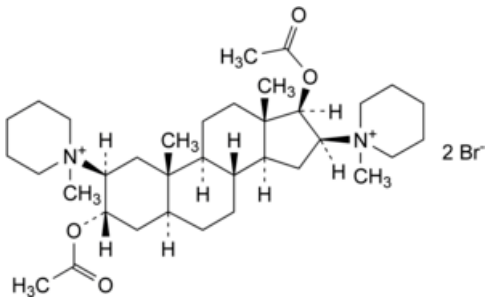
Edition: BP 2025 (Ph. Eur. 11.6 update)

Pancuronium Bromide

General Notices

(Ph. Eur. monograph 0681)



$C_{35}H_{60}Br_2N_2O_4$ 733 *15500-66-0*

Action and use

Non-depolarizing neuromuscular blocker.

Preparation

Pancuronium Injection

Ph Eur

DEFINITION

1,1′-[3α,17β-Bis(acetyloxy)-5α-androstane-2β,16β-diyl]bis(1-methylpiperidinium) dibromide.

Content

98.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance

White, yellowish-white or slightly pink, crystalline powder, hygroscopic.

Solubility

Very soluble or freely soluble in water, very soluble in methylene chloride, freely soluble in ethanol (96 per cent).

IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24).

Comparison pancuronium bromide CRS.

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

TESTS

Appearance of solution

The solution is clear (2.2.1) and colourless (2.2.2, Method II).

Dissolve 50 mg in water R and dilute to 25 mL with the same solvent.

Specific optical rotation (2.2.7)

+ 38.0 to + 42.0 (anhydrous substance).

Dissolve 0.75 g in water R and dilute to 25.0 mL with the same solvent.

Related substances

Thin-layer chromatography (2.2.27). *Prepare the solutions immediately before use.*

Test solution Dissolve 50.0 mg of the substance to be examined in methylene chloride R and dilute to 5.0 mL with the same solvent.

Reference solution (a) Dilute 1.0 mL of the test solution to 50.0 mL with methylene chloride R. Dilute 1.0 mL of this solution to 20.0 mL with methylene chloride R.

Reference solution (b) Dissolve 10.0 mg of pancuronium bromide for system suitability CRS (containing 1.0 per cent of impurity D) in 1.0 mL of methylene chloride R.

Plate TLC silica gel plate R (2-10 µm).

Mobile phase 400 g/L solution of sodium iodide R, acetonitrile R, 2-propanol R (5:10:85 *V/V/V*).

Application 5 µL.

Development In an unlined and unsaturated tank over a path of 8 cm.

Drying In a current of air at room temperature.

Detection Spray with a 20 g/L solution of sodium nitrite R and allow to dry for 5 min. Then spray with potassium iodobismuthate solution R5. Cover the plate with a transparent glass cover.

System suitability:

— the chromatogram obtained with reference solution (b) shows 2 clearly separated spots due to pancuronium bromide (R_F = about 0.5) and impurity D (R_F = about 0.6);

— the chromatogram obtained with reference solution (a) shows a clearly visible spot.

Note Impurity A if present will co-migrate with impurity D.

Limits:

— *impurities A, D*: any spot due to impurities A and/or D is not more intense than the spot due to impurity D in the chromatogram obtained with reference solution (b) (1.0 per cent),

— *unspecified impurities*: any other spot is not more intense than the spot in the chromatogram obtained with reference solution (a) (0.10 per cent).

Water (*2.5.12*)

Maximum 8.0 per cent, determined on 0.300 g.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.200 g in 50 mL of *acetic anhydride R*, heating if necessary. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* is equivalent to 36.63 mg of $C_{35}H_{60}Br_2N_2O_4$.

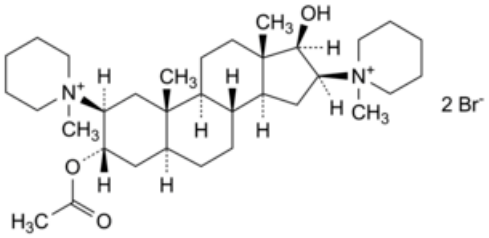
STORAGE

In an airtight container, protected from light.

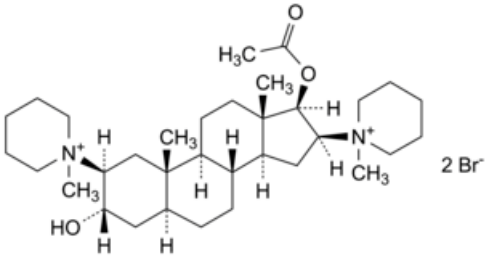
IMPURITIES

Specified impurities A, D.

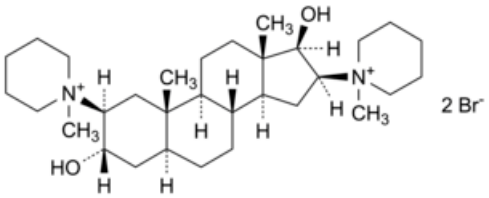
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) B, C, E.



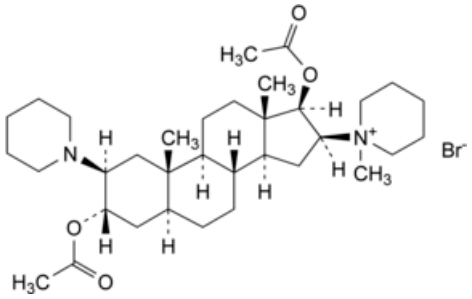
A. 1,1′-[3α-(acetyloxy)-17β-hydroxy-5α-androstane-2β,16β-diyl]bis(1-methylpiperidinium) dibromide (dacuronium bromide),



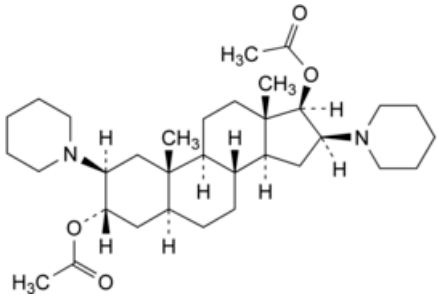
B. 1,1′-[17β-(acetyloxy)-3α-hydroxy-5α-androstane-2β,16β-diyl]bis(1-methylpiperidinium) dibromide,



C. 1,1′-(3α,17β-dihydroxy-5α-androstane-2β,16β-diyl)bis(1-methylpiperidinium) dibromide,



D. 1-[3α,17β-bis(acetyloxy)-2β-(piperidin-1-yl)-5α-androstan-16β-yl]-1-methylpiperidinium bromide (vecuronium bromide),



E. 2β,16β-bis(piperidin-1-yl)-5α-androstane-3α,17β-diyl diacetate.

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