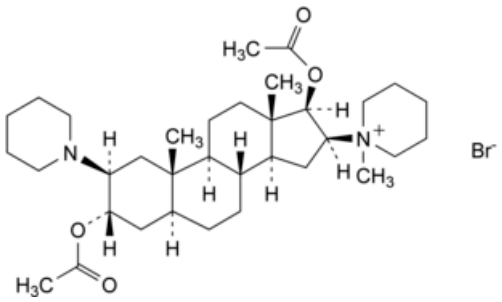
Edition: BP 2025 (Ph. Eur. 11.6 update)

Vecuronium Bromide

General Notices

(Ph. Eur. monograph 1769)



$C_{34}H_{57}BrN_2O_4$ 638 *50700-72-6*

Action and use

Non-depolarizing neuromuscular blocker.

Preparation

Vecuronium Bromide for Injection

Ph Eur

DEFINITION

1-[3α,17β-Bis(acetyloxy)-2β-(piperidin-1-yl)-5α-androstan-16β-yl]-1-methylpiperidin-1-ium bromide.

Content

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

CHARACTERS

Appearance

White or almost white crystals or crystalline powder.

Solubility

Slightly soluble in water, freely soluble in methylene chloride, sparingly soluble in acetonitrile and in anhydrous ethanol.

IDENTIFICATION

A. Specific optical rotation (see Tests).
B. Infrared absorption spectrophotometry (2.2.24).

Comparison *vecuronium bromide CRS*.

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

TESTS

Solution S

Dissolve 0.500 g in a 5.15 g/L solution of *hydrochloric acid R* and dilute to 50.0 mL with the same solution.

Appearance of solution

Solution S is clear (2.2.1) and not more intensely coloured than reference solution BY_7 (2.2.2, *Method II*).

Specific optical rotation (2.2.7)

+ 30.5 to + 35.0 (anhydrous substance), determined on solution S.

Impurity B

Thin-layer chromatography (2.2.27).

Test solution Dissolve 0.10 g of the substance to be examined in *methylene chloride R* and dilute to 5.0 mL with the same solvent.

Reference solution (a) Dissolve 5 mg of the substance to be examined and 5 mg of *pancuronium bromide CRS* (impurity B) in *methylene chloride R* and dilute to 5.0 mL with the same solvent.

Reference solution (b) Dissolve 5.0 mg of *pancuronium bromide CRS* (impurity B) in *methylene chloride R* and dilute to 100.0 mL with the same solvent.

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

Mobile phase Dissolve 1 g of *sodium bromide R* in 5 mL of *water R*. Add 85 mL of *2-propanol R*, then 10 mL of *acetonitrile R*.

Application 1 µL.

Development In an unsaturated tank, over 2/3 of the plate.

Drying In air for 30 min.

Detection Spray with a 2.5 g/L solution of *iodine R* in a mixture of equal volumes of *methanol R* and *methylene chloride R*.

System suitability Reference solution (a):

— the chromatogram shows 2 clearly separated spots.

Limit:

— *impurity B*: any spot due to impurity B is not more intense than the spot in the chromatogram obtained with reference solution (b) (0.25 per cent).

Related substances

Liquid chromatography (2.2.29). *Prepare the solutions immediately before use.*

Solution A 0.2 g/L solution of *hydrochloric acid R* in *methanol R2*.

Test solution Dissolve 40 mg of the substance to be examined in solution A and dilute to 20.0 mL with solution A.

Reference solution (a) Dissolve 4 mg of *vecuronium for system suitability CRS* (containing impurities C and E) in solution A and dilute to 2.0 mL with the solution A.

Reference solution (b) Dilute 1.0 mL of the test solution to 100.0 mL with solution A. Dilute 1.0 mL of this solution to 10.0 mL with solution A.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

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

— *temperature*: 40 °C.

Mobile phase Mix 135 volumes of an 18.0 g/L solution of *tetramethylammonium hydroxide R* previously adjusted to pH 6.9 with *phosphoric acid R*, 250 volumes of *methanol R2* and 615 volumes of *acetonitrile R1*.

Flow rate 2.0 mL/min.

Detection Spectrophotometer at 210 nm.

Autosampler Set at 4 °C.

Injection 20 µL.

Run time 5 times the retention time of vecuronium.

Identification of impurities Use the chromatogram supplied with *vecuronium for system suitability CRS* and the chromatogram obtained with reference solution (a) to identify the peaks due to impurities C and E.

Relative retention With reference to vecuronium (retention time = about 5 min): impurity C = about 0.8; impurity E = about 1.2.

System suitability:

— *signal-to-noise ratio*: minimum 28 for the principal peak in the chromatogram obtained with reference solution (b);

— *peak-to-valley ratio*: minimum 2.0, where H_p = height above the baseline of the peak due to impurity E and H_v = height above the baseline of the lowest point of the curve separating this peak from the principal peak in the chromatogram obtained with reference solution (a).

Calculation of percentage contents:

— *correction factor*: multiply the peak area of impurity C by 1.4;

— for each impurity, use the concentration of vecuronium bromide in reference solution (b).

Limits:

— *impurity C*: maximum 0.15 per cent;

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 0.2 per cent;

— *reporting threshold*: 0.05 per cent.

Water (2.5.12)

Maximum 4.0 per cent, determined on 0.300 g.

Sulfated ash (2.4.14)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.450 g in 50 mL of *glacial acetic acid R*. 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 63.8 mg of $C_{34}H_{57}BrN_2O_4$.

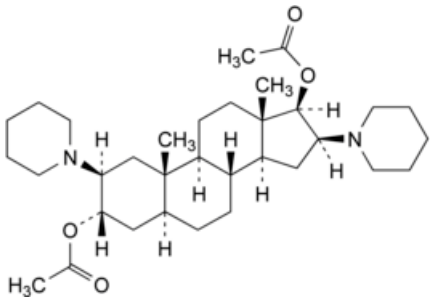
STORAGE

In an airtight container, protected from light and moisture.

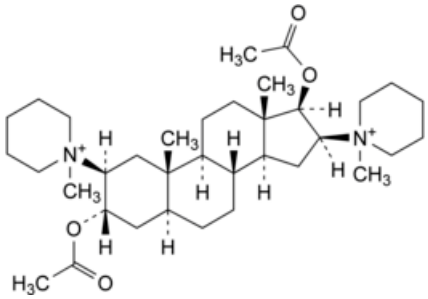
IMPURITIES

Specified impurities B, C.

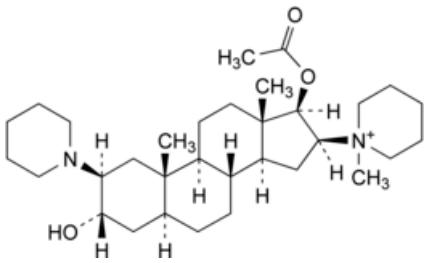
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical 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) A, D, E, F.



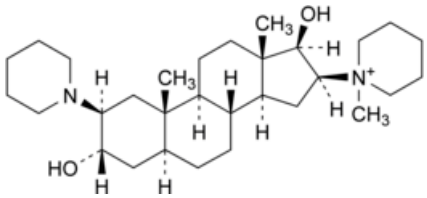
A. 2β,16β-di(piperidin-1-yl)-5α-androstane-3α,17β-diyl diacetate,



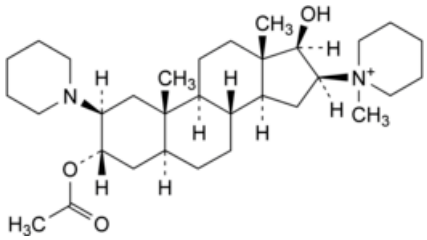
B. 1,1′-[3α,17β-bis(acetyloxy)-5α-androstane-2β,16β-diyl]bis(1-methylpiperidin-1-ium) (pancuronium),



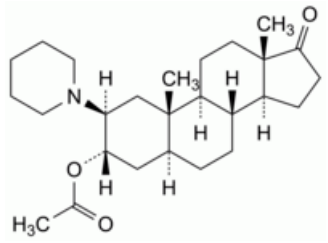
C. 1-[17β-(acetyloxy)-3α-hydroxy-2β-(piperidin-1-yl)-5α-androstan-16β-yl]-1-methylpiperidin-1-ium,



D. 1-[3α,17β-dihydroxy-2β-(piperidin-1-yl)-5α-androstan-16β-yl]-1-methylpiperidin-1-ium,



E. 1-[3α-(acetyloxy)-17β-hydroxy-2β-(piperidin-1-yl)-5α-androstan-16β-yl]-1-methylpiperidin-1-ium,



F. 2β-(piperidin-1-yl)-17-oxo-5α-androstan-3α-yl acetate.

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