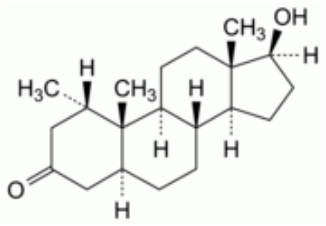
Edition: BP 2025 (Ph. Eur. 11.6 update)

Mesterolone

General Notices

(Ph. Eur. monograph 1730)



$C_{20}H_{32}O_2$ 304.5 *1424-00-6*

Action and use

Androgen.

Ph Eur

DEFINITION

17β-Hydroxy-1α-methyl-5α-androstan-3-one.

Content

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

CHARACTERS

Appearance

White or yellowish crystalline powder.

Solubility

Practically insoluble in water, sparingly soluble in acetone, in ethyl acetate and in methanol.

IDENTIFICATION

A. Melting point (2.2.14): 206 °C to 211 °C.
B. Infrared absorption spectrophotometry (2.2.24).

Comparison mesterolone CRS.

TESTS

Specific optical rotation (2.2.7)

+ 20 to + 24 (dried substance).

Dissolve 0.200 g in methylene chloride R and dilute to 10.0 mL with the same solvent.

Impurity B

Thin-layer chromatography (2.2.27).

Solvent mixture methanol R, methylene chloride R (50:50 *V/V*).

Test solution Dissolve 0.100 g of the substance to be examined in the solvent mixture and dilute to 10.0 mL with the solvent mixture.

Reference solution (a) Dilute 1.0 mL of the test solution to 200.0 mL with the solvent mixture.

Reference solution (b) Dissolve 5 mg of mesterolone impurity A CRS in reference solution (a) and dilute to 100 mL with the same solution.

Plate TLC silica gel plate R.

Mobile phase methanol R, acetone R, toluene R (2:15:85 *V/V/V*).

Application 10 µL.

Development Over 2/3 of the plate.

Drying In air.

Detection Examine in ultraviolet light at 366 nm; spray with a 200 g/L solution of toluenesulfonic acid R in ethanol (96 per cent) R and heat at 120 °C for 10 min.

System suitability The chromatogram obtained with reference solution (b) shows 2 clearly separated spots (blue spot due to mesterolone and yellow spot due to impurity A).

Limit:

— *impurity B*: any blue spot, apart from the principal spot, is not more intense than the spot in the chromatogram obtained with reference solution (a) (0.5 per cent).

Related substances

Liquid chromatography (2.2.29).

Solvent mixture water R, acetonitrile R (20:80 *V/V*).

Test solution Dissolve 50.0 mg of the substance to be examined in the solvent mixture and dilute to 25.0 mL with the solvent mixture.

Reference solution (a) Dissolve 50.0 mg of *mesterolone CRS* in the solvent mixture and dilute to 25.0 mL with the solvent mixture.

Reference solution (b) Dissolve 10 mg of *mesterolone for system suitability CRS* (containing impurity C) in the solvent mixture and dilute to 5 mL with the solvent mixture.

Reference solution (c) Dilute 1.0 mL of the test solution to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: *end-capped octadecylsilyl silica gel for chromatography R* (3 µm).

Mobile phase *acetonitrile R1*, *water for chromatography R*, *methanol R2* (20:40:60 *V/V/V*).

Flow rate 0.9 mL/min.

Detection Spectrophotometer at 200 nm.

Injection 50 µL of the test solution and reference solutions (b) and (c).

Run time 3 times the retention time of mesterolone.

Identification of impurities Use the chromatogram supplied with *mesterolone for system suitability CRS* and the chromatogram obtained with reference solution (b) to identify the peak due to impurity C.

Relative retention With reference to mesterolone (retention time = about 22 min): impurity C = about 0.9.

System suitability Reference solution (b):

— *resolution*: minimum 2.5 between the peaks due to impurity C and mesterolone.

Calculation of percentage contents:

— *correction factor*: multiply the peak area of impurity C by 0.2;

— for each impurity, use the concentration of mesterolone in reference solution (c).

Limits:

— *impurity C*: maximum 0.15 per cent;

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

— *total*: maximum 0.3 per cent;

— *reporting threshold*: 0.05 per cent.

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Liquid chromatography (2.2.29) as described in the test for related substances with the following modification.

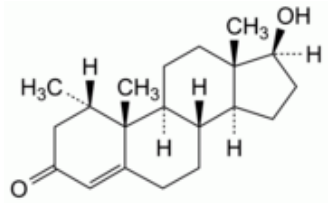
Injection 10 µL of the test solution and reference solution (a).

Calculate the percentage content of $C_{20}H_{32}O_2$ taking into account the assigned content of *mesterolone CRS*.

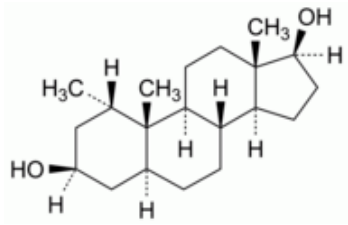
IMPURITIES

Specified impurities *B*, *C*.

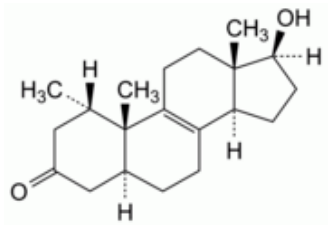
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical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



A. 17β-hydroxy-1α-methylandrost-4-en-3-one,



B. 1α-methyl-5α-androstane-3β,17β-diol,



C. 17β-hydroxy-1α-methyl-5α-androst-8-en-3-one.