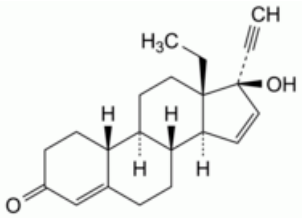
Edition: BP 2025 (Ph. Eur. 11.6 update)

Gestodene

General Notices

(Ph. Eur. monograph 1726)



$C_{21}H_{26}O_2$ 310.4 *60282-87-3*

Action and use

Progestogen.

Ph Eur

DEFINITION

13-Ethyl-17-hydroxy-18,19-dinor-17α-pregna-4,15-dien-20-yn-3-one.

Content

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

CHARACTERS

Appearance

White or yellowish, crystalline powder.

Solubility

Practically insoluble in water, freely soluble in methylene chloride, soluble in methanol, sparingly soluble in ethanol (96 per cent).

It shows polymorphism (*5.9*).

IDENTIFICATION

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

Comparison *gestodene CRS*.

If the spectra obtained in the solid state show differences, dissolve the substance to be examined and the reference substance separately in *acetone R*, evaporate to dryness and record new spectra using the residues.

TESTS

Specific optical rotation (2.2.7)

-188 to -198 (dried substance).

Dissolve 0.100 g in *methanol R* and dilute to 10.0 mL with the same solvent.

Related substances

Liquid chromatography (2.2.29).

Solvent mixture *acetonitrile R1*, *water R* (50:50 *V/V*).

Test solution (a) Dissolve 30.0 mg of the substance to be examined in 5 mL of *acetonitrile R1* and dilute to 10.0 mL with *water R*.

Test solution (b) Dilute 1.0 mL of test solution (a) to 10.0 mL with the solvent mixture.

Reference solution (a) Dissolve 3 mg of *gestodene for system suitability CRS* (containing impurities A, B, C and L) in 0.5 mL of *acetonitrile R1* and dilute to 1.0 mL with *water R*.

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

Reference solution (c) Dissolve 30.0 mg of *gestodene CRS* in 5 mL of *acetonitrile R1* and dilute to 10.0 mL with *water R*. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

Reference solution (d) Dissolve the contents of a vial of *gestodene impurity I CRS* in 1.0 mL of the solvent mixture.

Column:

— *size*: *l* = 0.15 m, Ø = 4.6 mm;

— *stationary phase*: spherical *end-capped octylsilyl silica gel for chromatography R* (3.5 µm).

Mobile phase:

— *mobile phase A*: *water R*;

— *mobile phase B*: *acetonitrile R1*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 2	62	38
2 - 20	62 → 58	38 → 42
20 - 24	58 → 30	42 → 70
24 - 32	30	70

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 205 nm and at 254 nm.

Injection 10 µL of test solution (a) and reference solutions (a), (b) and (d).

Identification of impurities Use the chromatogram supplied with *gestodene for system suitability CRS* and the chromatogram obtained with reference solution (a) to identify the peaks due to impurities A, B, C and L; use the chromatogram obtained with reference solution (d) to identify the peak due to impurity I.

Relative retention With reference to gestodene (retention time = about 12.5 min): impurity A = about 0.9; impurity C = about 1.1; impurity I = about 1.2; impurity L = about 1.46; impurity B = about 1.53.

System suitability Reference solution (a):

— *resolution*: minimum 2.0 between the peaks due to impurity A and gestodene.

Limits:

— *correction factors*: for the calculation of content, multiply the peak areas of the following impurities by the corresponding correction factor: impurity A = 2.2; impurity I = 1.3;

— *impurity A at 254 nm*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent);

— *impurity B at 205 nm*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent);

— *impurity C at 254 nm*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent);

— *impurities I, L at 205 nm*: for each impurity, not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.15 per cent);

— *unspecified impurities at 254 nm*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.10 per cent);

— *total at 254 nm*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent);

— *disregard limit at 254 nm*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (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 for 3 h.

ASSAY

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

Injection Test solution (b) and reference solution (c).

Detection Spectrophotometer at 254 nm.

Calculate the percentage content of $C_{21}H_{26}O_2$ from the declared content of *gestodene CRS*.

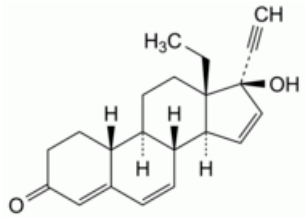
IMPURITIES

Specified impurities *A, B, C, I, L.*

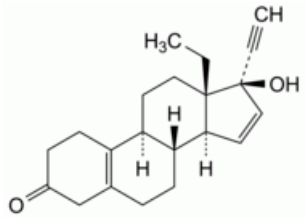
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical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

— *at 205 nm*: *G, J, K*;

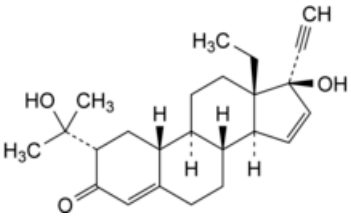
— *at 254 nm*: *D, E, F, H*.



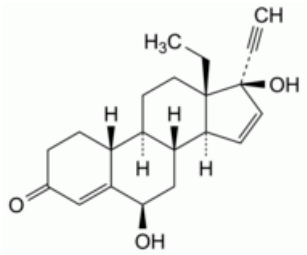
A. 13-ethyl-17-hydroxy-18,19-dinor-17α-pregna-4,6,15-trien-20-yn-3-one (Δ6-gestodene),



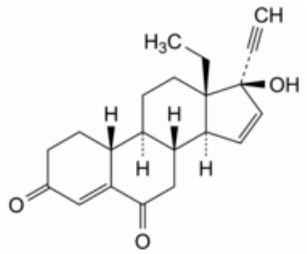
B. 13-ethyl-17-hydroxy-18,19-dinor-17α-pregna-5(10),15-dien-20-yn-3-one (Δ5(10)-gestodene),



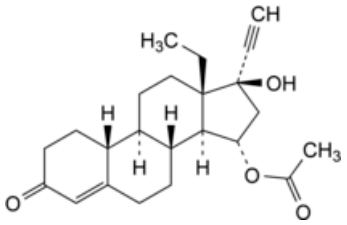
C. 13-ethyl-17-hydroxy-2α-(1-hydroxy-1-methylethyl)-18,19-dinor-17α-pregna-4,15-dien-20-yn-3-one (2-isopropanol-gestodene),



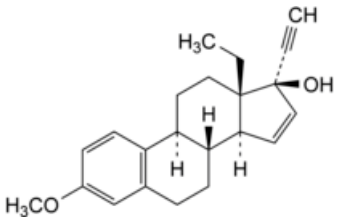
D. 13-ethyl-6β,17-dihydroxy-18,19-dinor-17α-pregna-4,15-dien-20-yn-3-one (6β-hydroxy-gestodene),



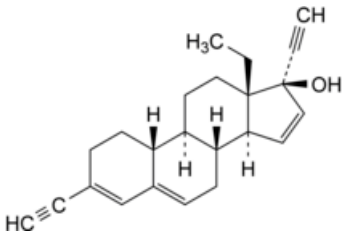
E. 13-ethyl-17-hydroxy-18,19-dinor-17α-pregna-4,15-dien-20-yne-3,6-dione (6-keto-gestodene),



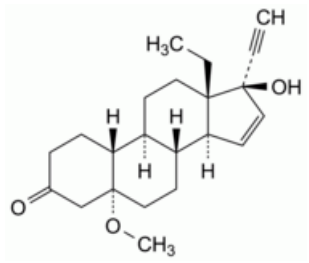
F. 13-ethyl-17-hydroxy-3-oxo-18,19-dinor-17α-pregn-4-en-20-yn-15α-yl acetate (15α-acetoxy-gestodene),



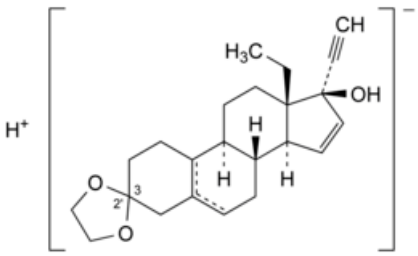
G. 13-ethyl-3-methoxy-18,19-dinor-17α-pregna-1,3,5(10),15-tetraen-20-yn-17-o1 (*A*-aromatic-gestodene),



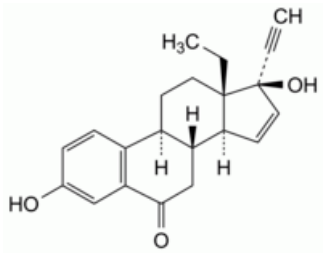
H. 13-ethyl-3-ethynyl-18,19-dinor-17α-pregna-3,5,15-trien-20-yn-17-o1 (diethynyl-gestodene),



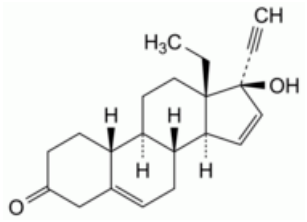
I. 13-ethyl-17-hydroxy-5-methoxy-18,19-dinor-5α,17α-pregn-15-en-20-yn-3-one (5-methoxy-gestodene),



J. 13-ethylspiro(18,19-dinor-17α-pregna-5,15-dien-20-yne-3,2′-[1,3]dioxolan)-17-ol and 13-ethylspiro(18,19-dinor-17α-pregna-5(10),15-dien-20-yne-3,2′-[1,3]dioxolan)-17-ol (gestodene ketal),



K. 13-ethyl-3,17-dihydroxy-18,19-dinor-17α-pregna-1,3,5(10),15-tetraen-20-yn-6-one (aromatic 6-keto-gestodene),



L. 13-ethyl-17-hydroxy-18,19-dinor-17α-pregna-5,15-dien-20-yn-3-one (Δ5(6)-gestodene).

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