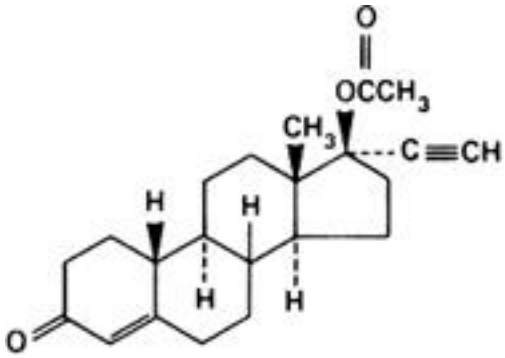
Norethisterone acetate (Norethisteroni acetas)

Molecular formula. $C_{22}H_{28}O_3$

Relative molecular mass. 340.5

Graphic formula.



Chemical name. 17-Hydroxy-19-nor-17*α*-pregn-4-en-20-yn-3-one acetate; 17-(acetyloxy)-19-nor-17*α*-pregn-4-en-20-yn-3-one; 17 *α*-ethynyl-17-hydroxyestr-4-en-3-one acetate; CAS Reg. No. 51-98-9.

Description. A white or creamy white, crystalline powder; odourless.

Solubility. Practically insoluble in water; soluble in 12.5 parts of ethanol (~750 g/l) TS and in 4 parts of acetone R; sparingly soluble in ether R.

Category. Progestational steroid.

Storage. Norethisterone acetate should be kept in a well-closed container, protected from light.

Requirements

Definition. Norethisterone acetate contains not less than 97.0% and not more than 103.0% of $C_{22}H_{28}O_3$, calculated with reference to the dried substance.

Identity tests

A. Carry out the examination as described under 1.7 Spectrophotometry in the infrared region. The infrared absorption spectrum is concordant with the spectrum obtained from norethisterone acetate RS or with the *reference spectrum* of norethisterone acetate.

B. See the test described under "Related substances". The principal spot obtained with solution B corresponds in position, appearance, and intensity with that obtained with solution C.

C. Heat 0.1 g with 2 mL of potassium hydroxide/ethanol (0.5 mol/l) VS in a water-bath for 5 minutes. Cool, add 2 mL of sulfuric acid (~700 g/l) TS and boil gently for 1 minute; ethyl acetate, perceptible by its odour (proceed with caution) is produced.

Specific optical rotation. Use a 20 mg/mL solution in dioxan R; $[\alpha]_D^{20\,°C}$ = -32° to -38°.

Sulfated ash. Not more than 1.0 mg/g.

Loss on drying. Dry to constant weight at 105°C; it loses not more than 5.0 mg/g.

Related substances. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using silica gel R1 as the coating substance and a mixture of equal volumes of toluene R and ethyl acetate R as the mobile phase. Apply separately to the plate 10 *µl*, in two portions of 5 *µl*, of each of 3 solutions in chloroform R containing (A) 10 mg of the test substance per mL, (B) 0.10 mg of the test substance per mL, and (C) 0.10 mg of norethisterone acetate RS per mL. After removing the plate from the chromatographic chamber, allow it to dry in air until the solvents have evaporated, and spray with sulfuric acid/ethanol TS. Heat the plate to 105°C for 15 minutes, allow to cool, and examine the chromatogram in daylight. Any spot obtained with solution A, other than the principal spot, is not more intense than that obtained with solution B.

Assay. Dissolve about 10 mg, accurately weighed, in sufficient ethanol (~750 g/l) TS to produce 100 mL; dilute 10.0 mL of this solution to 100 mL with the same solvent. Measure the absorbance of a 1-cm layer of the diluted solution at the maximum at about 240 nm. Calculate the amount of $C_{22}H_{28}O_3$ in the substance being tested by comparison with norethisterone acetate RS, similarly and concurrently examined. In an adequately calibrated spectrophotometer the absorbance of the reference solution should be 0.51 ± 0.03.