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Norethindrone Acetate

$C_{22}H_{28}O_3$ 340.46
19-Norpregn-4-en-20-yn-3-one, 17-(acetyloxy)-, (17α).

17-Hydroxy-19-nor-17α-pregn-4-en-20-yn-3-one acetate CAS RN®: 51-98-9; UNII: 9S44LIC7OJ.

» Norethindrone Acetate contains not less than 97.0 percent and not more than 103.0 percent of $C_{22}H_{28}O_3$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—
USP Norethindrone Acetate RS

Completeness of solution—The solution prepared for the determination of *Specific rotation* is clear and free from undissolved solids.

Change to read:

Identification, ▲*Spectroscopic Identification Tests ⟨197⟩, Infrared Spectroscopy: 197K*▲ (CN 1-May-2020) ·

Specific rotation ⟨781S⟩: between −32° and −38°.
Test solution: 20 mg per mL, in dioxane.

Loss on drying ⟨731⟩—Dry it at 105° for 3 hours: it loses not more than 0.5% of its weight.

Limit of ethynyl group—Proceed as directed in the test for *Ethynyl group* under *Norethindrone*. Not less than 7.13% and not more than 7.57% of ethynyl group is found.

Chromatographic purity—

TEST 1—

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture.

Test solution—Prepare a solution of Norethindrone Acetate in chloroform having a concentration of 10 mg per mL.

Standard stock solution—Prepare a solution of USP Norethindrone Acetate RS in chloroform having a known concentration of 10 mg per mL.

Standard solutions—Dilute accurately measured volumes of the *Standard stock solution* with chloroform to obtain *Standard solutions A*, *B*, *C*, and *D* having known concentrations of 150 µg per mL, 50 µg per mL, 30 µg per mL, and 10 µg per mL, respectively.

Application volume: 10 µL, as two 5-µL portions.

Developing solvent system: a mixture of toluene and ethyl acetate (1:1).

Procedure—Proceed as directed for *Thin-Layer Chromatography* under *Chromatography ⟨621⟩*, except to apply the solutions along a line 2.5 cm from the edge of the plate. Spray the plate with a mixture of methanol and sulfuric acid (7:3), and heat at 100° for 5 minutes. The *Test solution* exhibits a principal spot at the same R_F value as the principal spot of *Standard solution A*. Any individual secondary spot is not more intense than the spot in the chromatogram obtained from *Standard solution B:* not more than 0.5% of any individual impurity is found, and the total of impurities found is not more than 1.5%.

TEST 2—

Mobile phase—Prepare a filtered and degassed mixture of acetonitrile and water (6:4). Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Resolution solution—Dissolve accurately weighed quantities of desoxycorticosterone acetate and USP Norethindrone Acetate RS in *Mobile phase* to obtain a solution having concentrations of about 80 µg of each per mL.

Test solution—Transfer about 62.5 mg of Norethindrone Acetate, accurately weighed, to a 25-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix.

Diluted test solution—Transfer 1.0 mL of the *Test solution* to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see Chromatography ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 1 mL per minute. Chromatograph the *Resolution solution*, and record the peak

responses as directed for *Procedure:* the relative retention times are about 0.83 for desoxycorticosterone acetate and 1.0 for norethindrone acetate; and the resolution, *R,* between desoxycorticosterone acetate and norethindrone acetate is not less than 3.5.

Procedure—Separately inject equal volumes (about 20 µL) of the *Diluted test solution* and the *Test solution* into the chromatograph, record the chromatograms for twice the retention time of norethindrone acetate, and measure all of the peak areas. Calculate the percentage of each impurity in the portion of Norethindrone Acetate taken by the formula:

$$r_i/r_s$$

in which r_i is the peak area for each impurity obtained from the *Test solution;* and r_s is the sum of all the peaks obtained from the *Diluted test solution.* [NOTE—Exclude any peak having a response that is less than 0.025%.] Not more than 0.5% of any individual impurity is found; and not more than 1.0% of total impurities is found.

Assay—Transfer about 100 mg of Norethindrone Acetate, accurately weighed, to a 200-mL volumetric flask, add alcohol to volume, and mix. Transfer 5.0 mL of this solution to a 250-mL volumetric flask, dilute with alcohol to volume, and mix. Dissolve an accurately weighed quantity of USP Norethindrone Acetate RS in alcohol, and dilute quantitatively and stepwise with alcohol to obtain a Standard solution having a known concentration of about 10 µg per mL. Concomitantly determine the absorbances of both solutions in 1-cm cells at the wavelength of maximum absorbance at about 240 nm, with a suitable spectrophotometer, using alcohol as the blank. Calculate the quantity, in mg, of $C_{22}H_{28}O_3$ in the portion of Norethindrone Acetate taken by the formula:

$$10C(A_U/A_S)$$

in which C is the concentration, in µg per mL, of USP Norethindrone Acetate RS in the Standard solution, and A_U and A_S are the absorbances of the solution of Norethindrone Acetate and the Standard solution, respectively.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
NORETHINDRONE ACETATE	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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