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Norgestrel and Ethinyl Estradiol Tablets

» Norgestrel and Ethinyl Estradiol Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of norgestrel ($C_{21}H_{28}O_2$) and not less than 90.0 percent and not more than 110.0 percent of the labeled amount of ethinyl estradiol ($C_{20}H_{24}O_2$).

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—

USP Ethinyl Estradiol RS
USP Norgestrel RS

Identification—The retention times of the major peaks in the chromatogram of the *Assay preparation* correspond to those in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

Dissolution ⟨711⟩—

Medium: 0.0005% (w/v) polysorbate 80; 500 mL.

Apparatus 2: 75 rpm.

Time: 60 minutes.

Determine the amount of $C_{21}H_{28}O_2$ and $C_{20}H_{24}O_2$ dissolved by employing the following method. [Note—Do not use plastics during the preparation of solutions.]

Mobile phase—Prepare a filtered and degassed mixture of water and acetonitrile (3:2). Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Standard solution[Note—A volume of alcohol not exceeding 2% of the final volume of the solution may be used to aid in dissolving the USP Reference Standards.]—Dissolve an accurately weighed quantity of USP Norgestrel RS and USP Ethinyl Estradiol RS in *Medium,* and dilute quantitatively, and stepwise if necessary, with *Medium* to obtain a solution having known concentrations similar to those expected in the *Test solution*.

Test solution—Use a portion of the solution under test filtered through 0.7-µm borosilicate microfiber filter.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 247-nm detector (for norgestrel analysis), and a spectrofluorometric detector (for ethinyl estradiol analysis) with an excitation wavelength of about 285 nm and an emission wavelength of 310 nm, and a 4.6-mm × 15-cm column that contains packing L7. The flow rate is about 1 mL per minute. Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 0.7 for ethinyl estradiol and 1.0 for norgestrel; and the relative standard deviation for replicate injections is not more than 3.0% for the ethinyl estradiol and norgestrel peaks.

Procedure—Separately inject equal volumes (about 100 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantities, in mg, of norgestrel ($C_{21}H_{28}O_2$) and ethinyl estradiol ($C_{20}H_{24}O_2$) dissolved by the formula:

$$(500C)(r_U/r_S)$$

in which C is the concentration, in mg per mL, of the appropriate USP Reference Standard in the *Standard solution;* and r_U and r_S are the peak responses obtained from the *Test solution* and the *Standard solution,* respectively.

Tolerances—Not less than 75% *(Q)* of the labeled amount of $C_{21}H_{28}O_2$ and $C_{20}H_{24}O_2$ is dissolved in 60 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—

Mobile phase—Prepare a degassed mixture of water, acetonitrile, and methanol (45:35:15). Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Standard preparation—Dissolve an accurately weighed quantity of USP Norgestrel RS and USP Ethinyl Estradiol RS in *Mobile phase,* and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having known concentrations of about 100 µg of norgestrel per mL and 10 µg of ethinyl estradiol per mL.

Assay preparation—Transfer an accurately counted number of Tablets, equivalent to about 10 mg of norgestrel, to a 200-mL volumetric flask. Add 100.0 mL of *Mobile phase,* accurately measured, sonicate for 10 minutes to disintegrate the Tablets, and shake by mechanical means for

20 minutes. Centrifuge the clear portion of the solution at about 2000 rpm for 10 minutes, and filter the clear supernatant.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 215-nm detector and a 4.6-mm × 15-cm column that contains 5-µm packing L7. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the relative retention times are about 1.0 for ethinyl estradiol and 1.5 for norgestrel; the resolution, *R,* between the two major peaks is not less than 2.5; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 50 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of ethinyl estradiol ($C_{20}H_{24}O_2$) and norgestrel ($C_{21}H_{28}O_2$) in the portion of Tablets taken by the formula:

$$100C(r_U/r_S)$$

in which C is the concentration, in mg per mL, of the relevant USP Reference Standard in the *Standard preparation;* and r_U and r_S are the peak responses for the relevant analyte obtained from the *Assay preparation* and the *Standard preparation,* respectively.

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

Topic/Question	Contact	Expert Committee
NORGESTREL AND ETHINYL ESTRADIOL TABLETS	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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