Status: Currently Official on 16-Feb-2025
Official Date: Official Prior to 2013
Document Type: USP Monographs
DocId: GUID-52B10656-5CDB-4F3F-9C9A-4B6258CBF799_1_en-US
DOI: https://doi.org/10.31003/USPNF_M69910_01_01
DOI Ref: cig0o

Progesterone Intrauterine Contraceptive System

» Progesterone Intrauterine Contraceptive System contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{21}H_{30}O_2$. It is sterile.

Packaging and storage—Preserve in sealed, single-unit containers.

USP Reference standards ⟨11⟩—

USP Progesterone RS

Identification—Cut off and discard the sealed ends of the drug-containing cores of 2 Systems, and force the contents of the tubes into a small centrifuge tube. Add 3 mL of methanol, insert the stopper in the tube, mix, centrifuge, and transfer the clear, supernatant to a small beaker. Evaporate the methanol to dryness, wash the residue with two 4-mL portions of cyclohexane, and discard the washings. Dry the residue in vacuum at 50° to constant weight: the IR absorption spectrum of a mineral oil dispersion of the dried residue so obtained exhibits maxima only at the same wavelengths as that of a similar preparation of USP Progesterone RS.

Sterility Tests ⟨71⟩: meets the requirements.

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

Chromatographic purity—

Test solution—Remove the drug-containing core from 1 System, as directed in the *Assay*, transferring it to a small flask with 25 mL of methanol. Shake vigorously for several minutes, and allow the insoluble portion to settle. The resulting supernatant is the *Test solution*.

Procedure—Divide a 20- × 20-cm thin-layer chromatographic plate, coated with a 0.25-mm layer of chromatographic silica gel mixture, into sections 2 cm apart. In successive sections of the plate, on a line 2 cm from the lower edge of the plate and parallel to it, apply 1 µL, 2 µL, 3 µL, and 100 µL of the *Test solution*. Develop the plate in a suitable pre-equilibrated chromatographic chamber with a solvent system consisting of a mixture of chloroform and ethyl acetate (2:1) until the solvent front has moved 10 cm above the point of application of the spots. Remove the plate, and allow to air-dry. Observe the dried plate under short-wavelength UV light (254 nm). If spots other than the principal spot are observed in the lane of the 100-µL specimen, estimate the concentration of each by comparison with the 1-µL (1%), 2-µL (2%), and 3-µL (3%) spots. The requirement is met if the sum of impurities in the 100-µL specimen does not exceed 3%.

Drug release pattern—Remove the attached sutures from 10 Systems, and secure each system to a corrosion-resistant wire of sufficient length such that the systems are completely immersed during the shaking operation but do not touch the bottoms of the flasks. Suspend each system by the attached wire from the arm of a mechanical shaker designed to travel 2.5 cm in each direction in a vertically reciprocating cycle, at a speed of 2.5 cycles per second, so that each system is immersed in a separate 250-mL volumetric flask containing 230 mL of water, pre-equilibrated to 60 ± 0.1°. Immerse the volumetric flasks in an insulated constant-temperature water bath, maintained at 60 ± 0.1° and having a suitable means of maintaining the water level, so that the water level of the bath is above the water level in the flasks. Employ a rack or other suitable means of support for the flasks in the water bath.

Operate the shaker under the conditions described above for 23.5 hours, then remove the flasks and the systems from the bath. Remove the systems from the flasks, and immerse each system in a different flask containing 230 mL of water, pre-equilibrated to 60 ± 0.1°, and immerse these flasks in the water bath. Repeat this shaking operation daily for 12 days, using different flasks each day.

Determine the quantity of progesterone in the solutions from each of the 12 days of testing as follows. Immediately add 15 mL of methanol to each solution, allow to cool to room temperature, dilute with water to volume, and mix. Concomitantly determine the UV absorbances of each test solution and of a solution of USP Progesterone RS in the same medium, having a known concentration of about 7 µg per mL, in 2-cm cells at the wavelength of maximum absorbance at about 248 nm, with a suitable spectrophotometer, against a blank of water and methanol (47:3). Calculate the progesterone release rate, in mg per day, in the solutions taken by the formula:

$$(A_U/A_S)(24/23.5)0.25C$$

in which A_U and A_S are the absorbances of the test solution and the Standard solution, respectively; and C is the concentration, in µg per mL, of USP Progesterone RS in the Standard solution. For the time points specified, the drug-release pattern conforms to *Acceptance Table 1* under *Drug Release ⟨724⟩*.

Day	Release Rate (mg per day)
6	1.05–1.45
9	0.95–1.35
12	0.90–1.30

Assay—Cut off the lower sealed end of the drug-containing core of a number of Progesterone Intrauterine Contraceptive Systems, sufficient to provide about 400 mg of progesterone, forcing the viscous liquid core into a 1000-mL volumetric flask. Cut the core sections in half lengthwise, using a sharp blade, taking precautions not to contaminate either the core material or the outside of the membranes. Transfer all of these sections of the systems to the flask containing the core material. Add about 500 mL of methanol to the flask, shake vigorously for 5 to 10 minutes, dilute with methanol to volume, and centrifuge a portion of the solution. Dilute 10.0 mL of the clear, supernatant with methanol to 250 mL, and mix. Concomitantly determine the absorbances of this solution and of a Standard solution of USP Progesterone RS, previously dried and accurately weighed, in methanol having a known concentration of about 16 µg of progesterone per mL, in 1-cm cells at the wavelength of maximum absorbance at about 241 nm, with a suitable spectrophotometer, using methanol as the blank. Calculate the quantity, in mg, of $C_{21}H_{30}O_2$ in each System taken by the formula:

$$25(C/N)(A_U/A_S)$$

which C is the concentration, in µg per mL, of USP Progesterone RS in the Standard solution; N is the number of Systems taken; and A_U and A_S are the absorbances of the test solution and the Standard solution, respectively.

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

Topic/Question	Contact	Expert Committee
PROGESTERONE INTRAUTERINE CONTRACEPTIVE SYSTEM	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 31(1)

Current DocID: GUID-52B10656-5CDB-4F3F-9C9A-4B6258CBF799_1_en-US
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