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Progesterone Compounded Vaginal Inserts

DEFINITION

Progesterone Compounded Vaginal Inserts contain NLT 90.0% and NMT 110.0% of the labeled amount of progesterone ($C_{21}H_{30}O_2$).

Prepare Compounded Progesterone Vaginal Inserts in Fatty Acid Base or Polyethylene Glycol Base as follows (see *Pharmaceutical Compounding—Nonsterile Preparations* ⟨795⟩).

Progesterone (micronized)	25–600 mg
Fatty Acid Base or Polyethylene Glycol Base, a sufficient quantity to make	1 Insert

Calibrate the actual molds with the *Base* that is used for preparing the Inserts, and adjust the formula accordingly. Heat the *Base* slowly and evenly until melted. Slowly add the *Progesterone* powder to the melted base, with stirring. Mix thoroughly, and pour into molds. If preparing Inserts in *Fatty Acid Base*, cool in a refrigerator until solidified, trim, and wrap. If preparing Inserts in *Polyethylene Glycol Base*, cool, trim, and wrap.

ASSAY

• **Inserts in Fatty Acid Base**

Solution A: Dehydrated alcohol, isopropyl alcohol, and methanol (90:5:5)

Mobile phase: *Solution A* and water (55:45). Filter, and degas.

Diluent: *Solution A* and water (70:30)

System suitability stock solution A: 0.4 mg/mL of USP Methyltestosterone RS in *Mobile phase*

System suitability stock solution B: 0.4 mg/mL of USP Progesterone RS in *Mobile phase*

System suitability solution: Transfer 2.0 mL each of *System suitability stock solution A* and *System suitability stock solution B* to a 10-mL volumetric flask, and dilute with *Mobile phase* to volume.

Standard solution A: Prepare 0.25 mg/mL of USP Progesterone RS in *n*-propyl alcohol. Mix 5.0 mL of the solution with 10.0 mL of *Diluent*.

Standard solution B: Prepare 3 mg/mL of USP Progesterone RS in *n*-propyl alcohol. Transfer 3.0 mL of the solution to a 100-mL volumetric flask, and dilute with *Diluent* to volume.

Sample solution A: Transfer 1 Insert, containing NMT 100 mg of progesterone, to a 100-mL volumetric flask. Dissolve in 90 mL of *n*-propyl alcohol, heat at 45° for 4 min, and sonicate for 10 min. Cool, and dilute with *n*-propyl alcohol to volume. Dilute quantitatively, and stepwise if necessary, with *n*-propyl alcohol, sonicating if necessary, to obtain a solution containing a nominal concentration of 0.25 mg/mL of progesterone. Transfer 5.0 mL of this solution to a 50-mL centrifuge tube, add 10.0 mL of *Diluent*, sonicate for 1 min, and centrifuge for 10 min at 2000 rpm. Pass the supernatant through a filter of 0.45-µm or finer pore size, discarding the first 4 mL of the filtrate.

Sample solution B: Transfer 1 Insert, containing more than 100 mg of progesterone, to a 200-mL volumetric flask. Dissolve in 180 mL of *n*-propyl alcohol, heat at 45° for 8 min, and sonicate for 5 min. Cool, and dilute with *n*-propyl alcohol to volume. Dilute quantitatively, and stepwise if necessary, with *n*-propyl alcohol, sonicating each dilution for 1 min, to obtain a solution with a nominal concentration of 0.09 mg/mL of progesterone. Transfer 15 mL of this solution to a 50-mL centrifuge tube, and centrifuge for 10 min at 2000 rpm. Pass the supernatant through a filter of 0.45-µm or finer pore size, discarding the first 4 mL of the filtrate.

Chromatographic system

(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC

Detector: UV 245 nm

Column: 3.9-mm × 30-cm; packing L1

Column temperature: 40°

Flow rate: 1.0 mL/min

Injection volume: 10 µL

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for methyltestosterone and progesterone are about 0.8 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between methyltestosterone and progesterone

Tailing factor: NMT 2.0 for the progesterone peak

Relative standard deviation: NMT 2.0% for replicate injections for progesterone

Analysis

Samples: *Standard solution A* and *Sample solution A* or *Standard solution B* and *Sample solution B*

Calculate the percentage of the labeled amount of progesterone ($C_{21}H_{30}O_2$) in the Insert taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Progesterone RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of progesterone in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

• **Inserts in Polyethylene Glycol Base**

Solution A, Mobile phase, System suitability stock solution A, System suitability stock solution B, System suitability solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay* for *Inserts in Fatty Acid Base*.

Standard solution: 0.1 mg/mL of USP Progesterone RS in *Mobile phase*

Sample solution: Dissolve 1 Insert in 200 mL of *Mobile phase*, and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution with a nominal concentration of 0.1 mg/mL of progesterone. Pass a 10-mL portion of the mixture through a filter of 0.45-µm or finer pore size, discarding the first 4 mL of the filtrate.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of progesterone ($C_{21}H_{30}O_2$) in the Insert taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Progesterone RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of progesterone in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements for *Weight Variation*

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Package in light-resistant containers, and store in a refrigerator. Store Inserts in Fatty Acid Base in well-closed containers. Store Inserts in Polyethylene Glycol Base in tight containers, and do not dispense or store in polystyrene containers.

• **Beyond-Use Date:** NMT 90 days after the date on which they were compounded when stored in a refrigerator

• **Labeling:** Label Inserts to state whether they are Progesterone Vaginal Inserts in a Fatty Acid Base or in a Polyethylene Glycol Base. Label to state the amount of progesterone, in mg, in each Insert. Label to state that they are to be stored in a refrigerator. Label to state that wrappers are to be removed before use. If necessary, Inserts in Polyethylene Glycol Base may be moistened before insertion.

• **USP Reference Standards ⟨11⟩**

USP Methyltestosterone RS

USP Progesterone RS

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

Topic/Question	Contact	Expert Committee
PROGESTERONE COMPOUNDED VAGINAL INSERTS	Brian Serumaga Science Program Manager	CMP2020 Compounding 2020
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	CMP2020 Compounding 2020

Chromatographic Database Information: Chromatographic Database

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