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Hydroxyprogesterone Caproate Injection

DEFINITION

Hydroxyprogesterone Caproate Injection is a sterile solution of Hydroxyprogesterone Caproate in a suitable vegetable oil. It contains NLT 90.0% and NMT 110.0% of the labeled amount of hydroxyprogesterone caproate ($C_{27}H_{40}O_4$).

IDENTIFICATION

• **A.**

Sample solution: Transfer a volume of Injection, equivalent to 125 mg of hydroxyprogesterone caproate, to a 60-mL separator containing 10 mL of solvent hexane, 8 mL of methanol, and 2 mL of water. Insert the stopper, shake for 2 min, and allow the phases to separate. The lower layer is the *Sample solution*.

Analysis: To 3 mL of the *Sample solution* add sulfuric acid dropwise until a color develops, then add 3 mL of methanol.

Acceptance criteria: A purple color develops and the solution, when viewed under long-wavelength UV light, exhibits a pale yellow fluorescence.

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Mobile phase: Methanol and water (80:20)

Standard solution: 0.05 mg/mL of USP Hydroxyprogesterone Caproate RS in methanol

Sample solution: Nominally 0.05 mg/mL of hydroxyprogesterone caproate from an appropriate volume of Injection in methanol

Chromatographic system

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

Mode: LC

Detector: UV 242 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1.0 mL/min

Injection volume: 20 µL

Run time: Twice the retention time of hydroxyprogesterone caproate

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 4000 theoretical plates

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of hydroxyprogesterone caproate ($C_{27}H_{40}O_4$) in the portion of Injection 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 Hydroxyprogesterone Caproate RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• **Organic Impurities**

Mobile phase and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 0.5 µg/mL of USP Hydroxyprogesterone Caproate RS in methanol

Sample stock solution: Transfer 2.0 mL of Injection, equivalent to 500 mg of hydroxyprogesterone caproate, to a 100-mL volumetric flask and dilute with methanol to volume.

Sample solution: Nominally 0.25 mg/mL of hydroxyprogesterone caproate prepared as follows. Transfer an appropriate amount of *Sample stock solution* to a suitable volumetric flask and dilute with methanol to volume.

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 5.0%

Signal-to-noise ratio: NLT 10

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of hydroxyprogesterone or any individual unspecified degradation product in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each corresponding degradation product from the *Sample solution*

r_S = peak response of hydroxyprogesterone caproate from the *Standard solution*

C_S = concentration of USP Hydroxyprogesterone Caproate RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of hydroxyprogesterone caproate in the *Sample solution* (µg/mL)

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. Disregard any peak less than 0.05%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Hydroxyprogesterone[a]	0.4	1.3	1.0
Hydroxyprogesterone caproate	1.0	—	—
Individual unspecified degradation product	—	1.0	0.2
Total impurities	—	—	2.0

[a] 17-Hydroxypregn-4-ene-3,20-dione.

SPECIFIC TESTS

• **Water Determination ⟨921⟩, *Method I*:** NMT 0.2%

• **Other Requirements:** Meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose or in multiple-dose containers, preferably of Type I or Type III glass. Store at controlled room temperature.

• **USP Reference Standards ⟨11⟩**

USP Hydroxyprogesterone Caproate RS

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

Topic/Question	Contact	Expert Committee
HYDROXYPROGESTERONE CAPROATE INJECTION	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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