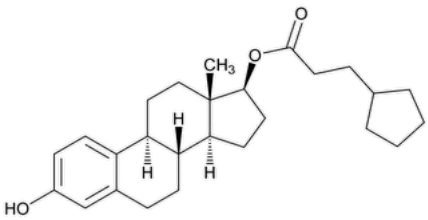
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-9529F5C8-A7CB-4018-8FAF-8DC944C961F4_2_en-US
DOI: https://doi.org/10.31003/USPNF_M30720_02_01
DOI Ref: 0hp8g

Estradiol Cypionate



$C_{26}H_{36}O_3$ 396.56

Estra-1,3,5(10)-triene-3,17-diol, (17β)-, 17-cyclopentanepropanoate;

Estradiol 17-cyclopentanepropionate CAS RN®: 313-06-4; UNII: 7E1DV054LO.

DEFINITION

Estradiol Cypionate contains NLT 97.0% and NMT 103.0% of estradiol cypionate ($C_{26}H_{36}O_3$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

• **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**

Solution A: Acetonitrile

Solution B: Water

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	70	30
25	70	30
30	100	0
40	100	0
41	70	30
50	70	30

System suitability solution: 1 mg/mL of USP Estradiol Cypionate System Suitability Mixture RS in acetonitrile

Standard solution: 1 mg/mL of USP Estradiol Cypionate RS in acetonitrile

Sample solution: 1 mg/mL of Estradiol Cypionate in acetonitrile

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 25-cm; 5-µm packing L26

Flow rate: 1 mL/min

Injection volume: 25 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between estradiol-9-ene cypionate and estradiol cypionate, *System suitability solution*

Relative standard deviation: NMT 1.10%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of estradiol cypionate ($C_{26}H_{36}O_3$) in the portion of Estradiol Cypionate 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 Estradiol Cypionate RS in the *Standard solution* (mg/mL)

C_U = concentration of Estradiol Cypionate in the *Sample solution* (mg/mL)

Acceptance criteria: 97.0%–103.0% on the dried basis

IMPURITIES

- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.2%
- **ORGANIC IMPURITIES**

Solution A, Solution B, Mobile phase, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 1 mg/mL of USP Estradiol Cypionate System Suitability Mixture RS and 2 µg/mL USP Estradiol RS in acetonitrile

Sensitivity solution: 0.5 µg/mL of USP Estradiol Cypionate RS in acetonitrile

Sample solution: 1 mg/mL of Estradiol Cypionate in acetonitrile

System suitability

Samples: *System suitability solution* and *Sensitivity solution*

Suitability requirements

[NOTE—See *Table 2* for the relative retention times.]

Resolution: NLT 1.5 between estradiol-9-ene cypionate and estradiol cypionate, *System suitability solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Estradiol Cypionate taken:

$$\text{Result} = (r_U/r_T) \times (1/F) \times 100$$

r_U = peak response for each impurity

r_T = sum of the responses of all the peaks

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. Disregard peaks that are less than 0.05% of the estradiol cypionate peak.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Estradiol	0.22	1.0	0.15
Estradiol-9-ene cypionate[a]	0.93	2.5	0.15
Estradiol cypionate	1.0	—	—
4-Methylestradiol cypionate[b]	1.3	1.0	0.15

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Estradiol dicypionate[c]	1.9	1.0	0.15
Any other individual unspecified impurity	—	1.0	0.10

[a] 3-Hydroxyestra-1,3,5(10),9(11)-tetraen-17β-yl cyclopentanepropanoate.

[b] 3-Hydroxy-4-methylestra-1,3,5(10)-trien-17β-yl cyclopentanepropanoate.

[c] Estra-1,3,5(10)-trien-3,17β-diyl di(cyclopentanepropanoate).

SPECIFIC TESTS

• **Optical Rotation,** *Specific Rotation* ⟨781S⟩

Sample solution: 20 mg/mL in dioxane

Acceptance criteria: +39° to +44°

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 4 h.

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

• **USP Reference Standards** ⟨11⟩

USP Estradiol RS

USP Estradiol Cypionate RS

USP Estradiol Cypionate System Suitability Mixture RS

This mixture contains:

Estradiol cypionate.

Estradiol-9-ene cypionate.

3-Hydroxyestra-1,3,5(10),9(11)-tetraen-17β-yl cyclopentanepropanoate. $C_{26}H_{34}O_3$ 394.55

Estradiol dicypionate.

Estra-1,3,5(10)-trien-3,17β-diyl di(cyclopentanepropanoate). $C_{34}H_{48}O_4$ 520.74

4-Methylestradiol cypionate.

3-Hydroxy-4-methylestra-1,3,5(10)-trien-17β-yl cyclopentanepropanoate. $C_{27}H_{38}O_3$ 410.59

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

Topic/Question	Contact	Expert Committee
ESTRADIOL CYPIONATE	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 39(6)

Current DocID: GUID-9529F5C8-A7CB-4018-8FAF-8DC944C961F4_2_en-US

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