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Clocortolone Pivalate Cream

DEFINITION

Clocortolone Pivalate Cream contains NLT 90.0% and NMT 110.0% of the labeled amount of clocortolone pivalate ($C_{27}H_{36}ClFO_5$) in a suitable cream base. It may contain suitable preservatives.

IDENTIFICATION

Delete the following:

▲• **Thin-Layer Chromatography**

Standard solution: 0.5 mg/mL of USP Clocortolone Pivalate RS in chloroform

Sample solution: Transfer the equivalent to 1 mg of clocortolone pivalate from Cream into a suitable separator. Add 5 mL of water, and extract with 10 mL of chloroform. Evaporate the chloroform layer to dryness, and dissolve the residue in 2 mL of methanol.

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 20 µL

Developing solvent system: Cyclohexane and ethyl acetate (2:1)

Analysis

Samples: *Standard solution* and *Sample solution*

Proceed as directed for *Chromatography ⟨621⟩, Thin-Layer Chromatography*. Apply 20 µL of the *Standard solution* and *Sample solution* about 1.5 cm from the bottom of the chromatographic plate. Allow the spots to dry and develop the chromatogram in the *Developing solvent system* until the solvent front has moved three-fourths of the length of the plate. Remove the plate from the developing chamber, mark the solvent front, and allow the solvent to evaporate. Locate the spots on the plate by viewing under short-wavelength UV light.

Acceptance criteria: The R_F value of the principal spot obtained from the *Sample solution* corresponds to that obtained from the *Standard solution*.▲ (USP 1-Aug-2022)

Add the following:

▲• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Aug-2022)

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Aug-2022)

ASSAY

Change to read:

• **Procedure**

▲**Mobile phase:** Acetonitrile and water (60:40)

Standard solution: 0.04 mg/mL of USP Clocortolone Pivalate RS in acetonitrile

Sample solution: Nominally 0.04 mg/mL of clocortolone pivalate from Cream in acetonitrile prepared as follows. Transfer a suitable amount of Cream to a suitable volumetric flask, add acetonitrile to 40% of the flask volume, and heat over a water bath at 60° for NLT 20 min to disperse the Cream. Cool to room temperature and dilute with acetonitrile to volume. Centrifuge to obtain a clear solution. [Note—A centrifuge speed of 4000 rpm for 10 min may be suitable.] Pass through a suitable filter of 0.2-µm pore size and use the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 240 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4-mm × 25-cm; 5-µm packing L1

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Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 5 µL

Run time: NLT 1.7 times the retention time of clocortolone pivalate

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of clocortolone pivalate ($C_{27}H_{36}ClFO_5$) in the portion of Cream taken:

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

r_U = peak response of clocortolone pivalate from the *Sample solution*

r_S = peak response of clocortolone pivalate from the *Standard solution*

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

C_U = nominal concentration of clocortolone pivalate in the *Sample solution* (mg/mL)▲ (USP 1-Aug-2022)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Minimum Fill ⟨755⟩:** Meets the requirements

Add the following:

▲IMPURITIES

• **Organic Impurities**

Mobile phase: Prepare as directed in the *Assay*.

System suitability solution: 0.15 mg/mL of USP Propylparaben RS and 1.6 µg/mL of USP Clocortolone RS in acetonitrile

Sensitivity solution: 0.16 µg/mL each of USP Clocortolone Pivalate RS and USP Clocortolone RS in acetonitrile

Standard solution: 0.32 µg/mL of USP Clocortolone Pivalate RS in acetonitrile

Sample solution: Nominally 0.16 mg/mL of clocortolone pivalate from Cream prepared as follows. Transfer a suitable amount of Cream to a suitable volumetric flask, add acetonitrile to 40% of the flask volume, and heat over a water bath at 60° for NLT 20 min to disperse the Cream. Cool to room temperature and dilute with acetonitrile to volume. Centrifuge to obtain a clear solution. [Note—A centrifuge speed of 4000 rpm for 10 min may be suitable.] Pass through a suitable filter of 0.2-µm pore size and use filtrate.

Chromatographic system: Proceed as directed in the *Assay* except for the *Injection volume* and *Run time*.

Injection volume: 10 µL

Run time: NLT 2.8 times the retention time of clocortolone pivalate

System suitability

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

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between propylparaben and clocortolone, *System suitability solution*

Relative standard deviation: NMT 5.0% each for clocortolone pivalate and clocortolone, *Sensitivity solution*

Signal-to-noise ratio: NLT 10 each for clocortolone pivalate and clocortolone, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Cream taken:

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

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of clocortolone pivalate from the *Standard solution*

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

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Clocortolone	0.25	0.2
Clocortolone pivalate	1.0	—
Any unspecified impurity	—	0.20
Total impurities	—	0.80

▲ (USP 1-Aug-2022)

SPECIFIC TESTS

• **pH** ⟨791⟩

Sample: 1-in-10 aqueous dispersion

Acceptance criteria: 5.0–7.0

• **Particle Size Determination**

Analysis: Place a small portion of Cream on a microscope slide, apply a cover slide, press slightly, and examine under 40× objective magnification using a suitable microscope equipped with polarized light. Scan the complete slide preparation, and record the size of the largest crystal found in reference to a calibrated grid.

Acceptance criteria: No particle in the Cream is greater than 50 µm when measured on the longitudinal axis.

Add the following:

▲• **Microbiological Examination of Nonsterile Products—Tests for Burkholderia Cepacia Complex** ⟨60⟩**:** Meets the requirements▲ (USP 1-Aug-2022)

Add the following:

▲• **Microbial Enumeration Tests** ⟨61⟩ and **Tests for Specified Microorganisms** ⟨62⟩**:** The total aerobic microbial count is NMT 10^2 cfu/g and the total combined molds and yeasts count is NMT 10^1 cfu/g. Meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa*.▲ (USP 1-Aug-2022)

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in collapsible tubes or in tight, light-resistant containers. ▲Store at controlled room temperature.▲ (USP 1-Aug-2022)

Change to read:

• **USP Reference Standards** ⟨11⟩

▲ USP Clocortolone RS

9-Chloro-6α-fluoro-11β,21-dihydroxy-16α-methylpregna-1,4-diene-3,20-dione.

$C_{22}H_{28}ClFO_4$ 410.91▲ (USP 1-Aug-2022)

USP Clocortolone Pivalate RS

▲ USP Propylparaben RS▲ (USP 1-Aug-2022)

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

Topic/Question	Contact	Expert Committee
CLOCORTOLONE PIVALATE CREAM	Documentary Standards Support	SM52020 Small Molecules 5

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Chromatographic Database Information: Chromatographic Database

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