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Clobetasol Propionate Ointment

DEFINITION

Clobetasol Propionate Ointment is Clobetasol Propionate in a suitable ointment base. It contains NLT 90.0% and NMT 115.0% of the labeled amount of clobetasol propionate ($C_{25}H_{32}ClFO_5$).

IDENTIFICATION

Delete the following:

▲• **A.** **Thin-Layer Chromatographic Identification Test** ⟨201⟩

Standard solution: 0.5 mg/mL of of USP Clobetasol Propionate RS in chloroform

Test solution: Nominally 0.5 mg/mL of clobetasol propionate. Transfer a portion of Ointment equivalent to 1.0 mg of clobetasol propionate to a 25-mL, plastic-stoppered centrifuge tube. Add 10 mL of methanol, and cap. Heat in a 70° water bath for 4 min, remove the tube from the bath, and shake vigorously. Repeat the heating and shaking. Freeze the mixture in an ice bath for 5 min, and centrifuge at about 3500 rpm for 10 min. Transfer 5 mL of the supernatant to a suitable vial. Evaporate with the aid of a stream of nitrogen to dryness. Dissolve the residue in 1.0 mL of chloroform.

Developing solvent system: Chloroform, acetone, and alcohol (100:10:5)

Acceptance criteria: The R_F value of the principal spot obtained from the *Test solution* corresponds to that from the *Standard solution*. ▲ (USP 1-May-2021)

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-May-2021)

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-May-2021)

ASSAY

Change to read:

• **Procedure**

▲**Buffer:** 6 g/L of monobasic sodium phosphate. Adjust with phosphoric acid to a pH of 2.5.

Mobile phase: Acetonitrile, methanol, and *Buffer* (475:100:425)

Solution A: Absolute alcohol and methanol (95:5)

Internal standard solution: 0.06 mg/mL of USP Beclomethasone Dipropionate RS in *Solution A*

System suitability solution: 0.066 mg/mL of USP Clobetasol Propionate RS and 2.6 µg/mL of USP Clobetasol Propionate Related Compound A RS in *Internal standard solution*

Standard solution: 0.066 mg/mL of USP Clobetasol Propionate RS in *Internal standard solution*

Sample solution: Nominally 0.066 mg/mL of clobetasol propionate in *Internal standard solution* prepared as follows. Transfer a suitable amount of Ointment equivalent to 1.65 mg of clobetasol propionate to a 50-mL glass centrifuge tube with a screw cap having a Teflon liner. Pipet 25 mL of *Internal standard solution*, and heat in a water bath at 70° for NLT 10 min with intermittent short vortexing. After heating, mix the sample on a vortex mixer for NLT 30 s and cool in an ice bath for NLT 10 min. Repeat the heating, vortexing, and cooling cycle two more times. Allow the contents to reach room temperature for a minimum of 30 min. Pass a portion through a suitable filter of 0.45-µm pore size, discarding the first 5 mL of 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 210–350 nm.

Column: 4.6-mm × 15-cm; 2.6-µm packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 3 times the retention time of clobetasol propionate

System suitability

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

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

Suitability requirements

Resolution: NLT 1.5 between clobetasol propionate and clobetasol propionate related compound A, *System suitability solution*

Tailing factor: NMT 2.0 for both the clobetasol propionate and beclomethasone dipropionate peaks, *System suitability solution*

Relative standard deviation: NMT 2.0% for the area ratio of clobetasol propionate to beclomethasone dipropionate, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of clobetasol propionate ($C_{25}H_{32}ClFO_5$) in the portion of Ointment taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak area ratio of clobetasol propionate to beclomethasone dipropionate from the *Sample solution*

R_S = peak area ratio of clobetasol propionate to beclomethasone dipropionate from the *Standard solution*

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

C_U = nominal concentration of clobetasol propionate in the *Sample solution* (mg/mL)▲ (USP 1-May-2021)

Acceptance criteria: 90.0%–115.0%

IMPURITIES

Add the following:

▲• **ORGANIC IMPURITIES**

Buffer, Mobile phase, Solution A, Internal standard solution, System suitability solution, Standard solution, Sample solution, and

Chromatographic system: Proceed as directed in the *Assay*.

Sensitivity solution: 0.066 µg/mL of USP Clobetasol Propionate RS in *Internal standard solution*

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between clobetasol propionate and clobetasol propionate related compound A, *System suitability solution*

Tailing factor: NMT 2.0 for the clobetasol propionate and beclomethasone dipropionate peaks, *System suitability solution*

Relative standard deviation: NMT 2.0% for the area ratio of clobetasol propionate to beclomethasone dipropionate, *Standard solution*

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

Analysis

Sample: *Sample solution*

Calculate the percentage of each degradation product in the portion of Ointment taken:

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

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

r_T = sum of the peak responses of clobetasol propionate and all the degradation products from the *Sample solution*

F = relative response factor for each individual degradation product (see *Table 1*)

Acceptance criteria: See *Table 1*. The reporting threshold is 0.1%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Clobetasol[a]	0.5	1.1	1.0
Clobetasol propionate	1.0	—	—
Clobetasol propionate related compound A	1.1	1.0	4.0
Beclomethasone dipropionate[b]	1.5	—	—
Any individual unspecified degradation product	—	1.0	1.0
Total degradation products	—	—	4.0▲ (USP 1-May-2021)

[a] 21-Chloro-9-fluoro-11β,17-dihydroxy-16β-methylpregna-1,4-diene-3,20-dione.

[b] Internal standard.

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count does not exceed 10^2 cfu/g. It meets the requirements of the tests for absence of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Salmonella* species.

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

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in collapsible tubes or in tight containers. Store at controlled room temperature. Do not refrigerate.

Change to read:

• **USP Reference Standards ⟨11⟩**

▲USP Beclomethasone Dipropionate RS▲ (USP 1-May-2021)

USP Clobetasol Propionate RS

USP Clobetasol Propionate Related Compound A RS

▲(17*R*)-4'-Chloro-5'-ethyl-9-fluoro-11β-hydroxy-16β-methylspiro[androsta-1,4-diene-17,2'(3'*H*)-furan]-3,3'-dione.▲ (USP 1-May-2021)

$C_{25}H_{30}ClFO_4$ 448.96

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

Topic/Question	Contact	Expert Committee
CLOBETASOL PROPIONATE OINTMENT	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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