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Add the following:

▲Calcipotriene Cream

DEFINITION
Calcipotriene Cream contains NLT 90.0% and NMT 110.0% of the labeled amount of calcipotriene ($C_{27}H_{40}O_3$).

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

ASSAY
• **Procedure**
Protect solutions containing calcipotriene from light and air. Prepare the solutions containing calcipotriene NMT 1 h before use.

Solution A: 0.132 g/mL of monobasic ammonium phosphate in water

Mobile phase: Methanol and water (70:30)

Diluent: Methanol, *Solution A*, and water (70: 0.3: 29.7)

Standard stock solution: 0.1 mg/mL of USP Calcipotriene RS in *Diluent*. Sonicate if necessary.

Standard solution: 2.0 µg/mL of USP Calcipotriene RS prepared as follows. Transfer 5 mL of *Standard stock solution* into a 250-mL volumetric flask, add 50 mL of tetrahydrofuran, and dilute with *Diluent* to volume.

Sample stock solution: Nominally equivalent to 0.01 mg/mL of calcipotriene in tetrahydrofuran prepared as follows. Transfer Cream nominally equivalent to 0.25 mg of calcipotriene to a 25-mL volumetric flask. Add 10 mL of tetrahydrofuran and sonicate for 20 min with intermittent shaking. Cool to room temperature and dilute with tetrahydrofuran to volume.

Sample solution: Nominally equivalent to 2.0 µg/mL of calcipotriene prepared as follows. Transfer 5 mL of *Sample stock solution* into a suitable container. Add 20 mL of *Diluent*, mix, and sonicate for 15 min. Pass through a Teflon filter of 0.45-µm pore size and discard the first few milliliters of the filtrate.

Chromatographic system
(See *Chromatography ⟨621⟩, System Suitability*.)
Mode: LC
Detector: UV 264 nm. For *Identification B*, use a diode array detector in the range of 190–400 nm.
Column: 4.6-mm × 15-cm; 3-µm packing L1
Flow rate: 1.0 mL/min
Injection volume: 50 µL

System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 2.0
Relative standard deviation: NMT 2.0%

Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of calcipotriene ($C_{27}H_{40}O_3$) in the portion of Cream taken:

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

r_U = peak response of calcipotriene from the *Sample solution*

r_S = peak response of calcipotriene from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

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

IMPURITIES

• **Organic Impurities**

Protect solutions containing calcipotriene from light and air. Prepare the *Standard solution* and the *Sample solution* NMT 1 h before use.

Prepare the *System suitability solution* daily.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Water (%)	Methanol (%)
0	35	65
45	35	65
55	25	75
60	15	85
70	15	85
75	35	65
85	35	65

Diluent: Prepare as directed in the *Assay*.

System suitability stock solution: 0.125 mg/mL of USP Calcipotriene RS and 2.0 µg/mL of USP Calcipotriene Related Compound C RS in *Diluent*

System suitability solution: 0.0125 mg/mL of USP Calcipotriene RS and 0.2 µg/mL of USP Calcipotriene Related Compound C RS prepared as follows. Transfer 1 mL of *System suitability stock solution* to a 10-mL volumetric flask. Add 1 mL of tetrahydrofuran and dilute with *Diluent* to volume.

Standard stock solution: 62.5 µg/mL of USP Calcipotriene RS prepared as follows. Transfer an appropriate amount of USP Calcipotriene RS to a suitable volumetric flask, add *Diluent* equivalent to 50% of the final volume, and sonicate to dissolve. Further add tetrahydrofuran equivalent to 25% of the final volume and dilute with *Diluent* to volume.

Standard solution: 0.125 µg/mL of USP Calcipotriene RS in *Diluent*, from *Standard stock solution*

Sensitivity solution: 0.0125 µg/mL of USP Calcipotriene RS in *Diluent*, from *Standard solution*

Sample solution: Nominally 0.0125 mg/mL of calcipotriene prepared as follows. Transfer Cream equivalent to 0.25 mg of calcipotriene to a 20-mL volumetric flask and add 5 mL of tetrahydrofuran. Sonicate for 15 min with intermittent shaking. Cool to room temperature and dilute with *Diluent* to volume. Place the volumetric flask in a beaker containing ice-cold water for 2–3 min, and pass the solution through a 0.45-µm Teflon filter. Discard the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 264 nm

Column: 4.6-mm × 15-cm; 3-µm packing L1

Column temperature: 30°

Flow rate: 1.0 mL/min

Injection volume: 100 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.2 between calcipotriene related compound C and calcipotriene, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

r_S = peak response of calcipotriene from the *Standard solution*

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

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

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

Acceptance criteria: See *Table 2*. The reporting threshold is 0.1%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Calcipotriene related compound C	0.96	1.2	2.0
Calcipotriene	1.0	—	—
Calcipotriene impurity D[a]	1.09	1.0	3.6
Any individual unspecified degradation product	—	1.0	0.7
Total degradation products	—	—	4.6

[a] (5*Z*,7*E*,22*E*,24*R*)-24-Cyclopropyl-9,10-secochola-5,7,10(19),22-tetraene-1α,3β,24-triol.

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count is NMT 10^2 cfu/g. The total yeasts and molds count is NMT 10^1 cfu/g. It meets the requirements of the tests for the absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa* species.

• **pH ⟨791⟩**
Sample solution: 10 g of Cream in 100 mL of water
Acceptance criteria: 7.0–8.5

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers, and store at controlled room temperature. Do not freeze.

• **USP Reference Standards ⟨11⟩**
USP Calcipotriene RS
USP Calcipotriene Related Compound C RS

(5*E*,7*E*,22*E*,24*S*)-24-Cyclopropyl-9,10-secochola-5,7,10(19),22-tetraene-1α,3β,24-triol.
$C_{27}H_{40}O_3$ 412.60▲ (USP 1-Dec-2021)

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

Topic/Question	Contact	Expert Committee
CALCIPOTRIENE CREAM	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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