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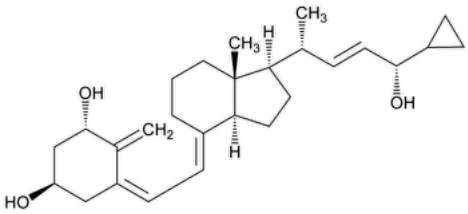
Calcipotriene

Change to read:



$C_{27}H_{40}O_3$ 412.60

9,10-Secochola-5,7,10(19),22-tetraene-1,3,24-triol, 24-cyclopropyl-, (1α,3β,5*Z*,7*E*,22*E*,24*S*)-;

(5*Z*,7*E*,22*E*,24*S*)-24-Cyclopropyl-9,10-secochola-5,7,10(19),22-tetraene-1α,3β,24-triol CAS RN®: 112965-21-6; UNII: 143NQ3779B.

▲Monohydrate

$C_{27}H_{40}O_3 \cdot H_2O$ 430.63 CAS RN®: 147657-22-5.▲ (USP 1-May-2021)

DEFINITION

Change to read:

▲Calcipotriene is anhydrous or contains one molecule of water of hydration. The anhydrous form contains NLT 97.0% and NMT 102.0% of calcipotriene ($C_{27}H_{40}O_3$), calculated on the dried basis. The monohydrate form contains NLT 96.0% and NMT 102.0% of calcipotriene ($C_{27}H_{40}O_3$), calculated on the anhydrous and solvent-free basis.▲ (USP 1-May-2021)

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K
- **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

Change to read:

- **Procedure**

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.

Buffer: 1.0 g/L of tris(hydroxymethyl)aminomethane adjusted with phosphoric acid to a pH of 7.25 ± 0.25

Mobile phase: Acetonitrile and *Buffer* (45:55)

System suitability solution: 0.1 mg/mL of USP Calcipotriene RS and 0.01 mg/mL of USP Calcipotriene Related Compound C RS in *Mobile phase*

Standard solution: 0.1 mg/mL of USP Calcipotriene RS dissolved in 10% of acetonitrile and then diluted in *Mobile phase*

Sample solution: 0.1 mg/mL of Calcipotriene dissolved in 10% of acetonitrile and then diluted in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 264 nm

Column: 4.0-mm × 25-cm; 5-µm packing L7

Autosampler temperature: 4°

Flow rate: 1.0 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution*▲and *Standard solution*▲ (USP 1-May-2021)

[Note—The relative retention times for calcipotriene related compound C and calcipotriene are 0.94 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between calcipotriene related compound C and calcipotriene, ▲*System suitability solution*▲ (USP 1-May-2021)

Relative standard deviation: NMT 1.0%, ▲*Standard solution*▲ (USP 1-May-2021)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of calcipotriene ($C_{27}H_{40}O_3$) in the portion of Calcipotriene 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 = concentration of Calcipotriene in the *Sample solution* (mg/mL)

Acceptance criteria

▲**Labeled as anhydrous form:** 97.0%–102.0% on the dried basis

Labeled as monohydrate form: 96.0%–102.0% on the anhydrous and solvent-free basis▲ (USP 1-May-2021)

IMPURITIES

Change to read:

• **Organic Impurities, Procedure 1: HPLC**

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.

Buffer, Mobile phase, System suitability solution, and **Chromatographic system**▲▲ (USP 1-May-2021) **:** Proceed as directed in the *Assay*.

Standard stock solution: Use the *Standard solution* in the *Assay*.

Standard solution: 0.004 mg/mL of USP Calcipotriene RS in *Mobile phase*, from the *Standard stock solution*

▲**Sensitivity solution:** 0.2 µg/mL of USP Calcipotriene RS in *Mobile phase*, from *Standard solution*▲ (USP 1-May-2021)

Sample solution: 0.4 mg/mL of Calcipotriene dissolved in 10% of acetonitrile and then diluted in *Mobile phase*

▲**System suitability**

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

[Note—The relative retention times for calcipotriene related compound C and calcipotriene are 0.94 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 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*▲ (USP 1-May-2021)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any impurity in the portion of Calcipotriene taken:

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

r_U = peak response of any 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 = concentration of Calcipotriene in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 1*. ▲The reporting threshold is 0.05%.▲ (USP 1-May-2021)

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
▲Calcipotriene impurity B[a]	0.83	0.5▲ (USP 1-May-2021)
Calcipotriene related compound C[b]	0.92–0.96	▲1.0▲ (USP 1-May-2021)
Calcipotriene	1.00	—

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Calcipotriene impurity D[c]	1.13–1.17	▲1.0▲ (USP 1-May-2021)
Any individual unspecified impurity	—	0.10
Total impurities	—	▲2.5▲ (USP 1-May-2021)

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

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

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

Change to read:

• **Organic Impurities, Procedure 2: TLC**

Prepare solutions containing calcipotriene in low-actinic glassware, and protect from air. Carry out the test as rapidly as possible.

Diluent: Chloroform and triethylamine (9:1)

System suitability solution: 10 mg/mL of USP Calcipotriene RS in *Diluent*. Heat in a water bath at 60° for 2 h to form ▲*pre*-Calcipotriene.▲ (USP 1-May-2021)

Standard solution 1: 0.025 mg/mL of USP Calcipotriene RS in *Diluent* (0.25%)

Standard solution 2: 0.01 mg/mL of USP Calcipotriene RS in *Diluent* (0.10%)

▲**Standard solution 3:** 0.05 mg/mL of USP Calcipotriene RS in *Diluent* (0.5%)▲ (USP 1-May-2021)

Sample solution: 10 mg/mL of Calcipotriene in *Diluent*

Developing solvent system: Methylene chloride and isobutyl alcohol (80:20)

Chromatographic system

(See *Chromatography ⟨621⟩, General Procedures, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic plate coated with silica gel mixture

Application volume: 10 µL

Spray reagent: Transfer 20 mL of sulfuric acid into a 100-mL volumetric flask, and dilute with alcohol to volume.

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: The secondary spot ▲*pre*-Calcipotriene▲ (USP 1-May-2021) and principle spot calcipotriene are clearly separated.

Analysis

Samples: *Standard solution 1*, *Standard solution 2*, ▲*Standard solution 3*,▲ (USP 1-May-2021) and *Sample solution*

Develop with *Developing solvent system* until the solvent system has moved two-thirds of the plate from the point of spotting. Remove the plate, and let the plate air-dry. Dry it again at 140° for 10 min followed by spraying the hot plate with the *Spray reagent*. Dry the plate for NMT 1 min at 140°. Examine the plate under UV light at 366 nm.

Acceptance criteria: The spot of any impurity in the *Sample solution* is not more intense than the spot of calcipotriene in the appropriate *Standard solution* specified in *Table 2*.

Table 2

Name	Relative Retardation (R_{ret})	Comparison Solution	Acceptance Criteria, NMT (%)
Calcipotriene impurity G[a] and calcipotriene impurity H[b]	0.4	*Standard solution 1*	0.25
▲*pre*-Calcipotriene▲ (USP 1-May-2021) [c]	0.9	▲*Standard solution 3*▲ (USP 1-May-2021)	▲0.5▲ (USP 1-May-2021)
Calcipotriene	1.0	—	—

Name	Relative Retardation (R_{ret})	Comparison Solution	Acceptance Criteria, NMT (%)
Calcipotriene impurity A[d]	1.2	*Standard solution 1*	0.25
Any other individual impurity	—	*Standard solution 2*	0.10

[a] 24,24'-Oxybis[(5*Z*,7*E*,22*E*,24*S*)-24-cyclopropyl-9,10-secochola-5,7,10(19),22-tetraene-1α,3β-diol].

[b] (5*Z*,7*E*,22*E*,24*R*)-24-Cyclopropyl-24-{[(5*Z*,7*E*,22*E*,24*S*)-24-cyclopropyl-1α,3β-dihydroxy-9,10-secochola-5,7,10(19),22-tetraen-24-yl]oxy}-9,10-secochola-5,7,10(19),22-tetraene-1α,3β-diol.

[c] (5*E*,6*E*,22*E*,24*S*)-24-Cyclopropyl-9,10-secochola-5(10),6,22-triene-1α,3β,24-triol.

[d] (5*Z*,7▲*E*▲ (USP 1-May-2021) ,22*E*)-24-Cyclopropyl-9,10-secochola-5,7,10(19),22-tetraene-24-one-1α,3β-diol.

SPECIFIC TESTS

Change to read:

• **Loss on Drying** ▲(where it is labeled as anhydrous form)▲ (USP 1-May-2021)

(See *Thermal Analysis* ⟨891⟩.)

Sample: 5 mg

Analysis: Heat the *Sample* to 105° at a rate of 10°/min, and hold at 105° for 60 min.

Acceptance criteria: NMT 1.0%

Add the following:

▲• **Water Determination** ⟨921⟩, *Method I*(where it is labeled as monohydrate form)**:** 3.3%–5.0%▲ (USP 1-May-2021)

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in tight containers. ▲If labeled as anhydrous form,▲ (USP 1-May-2021) store at 2°–8° or at −20° or below. ▲If labeled as monohydrate form, store at room temperature.▲ (USP 1-May-2021) Protect from light.

Add the following:

▲• **Labeling:** Label it to indicate whether it is the anhydrous form or the monohydrate form.▲ (USP 1-May-2021)

Change to read:

• **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.

$C_{27}H_{40}O_3$ ▲412.61▲ (USP 1-May-2021)

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

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

Chromatographic Database Information: Chromatographic Database

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