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Add the following:

▲Calcipotriene and Betamethasone Dipropionate Ointment

DEFINITION

Calcipotriene and Betamethasone Dipropionate Ointment contains NLT 90.0% and NMT 114.0% of the labeled amount of calcipotriene ($C_{27}H_{40}O_3$) and NLT 90.0% and NMT 110.0% of the labeled amount of betamethasone dipropionate ($C_{28}H_{37}FO_7$) in a suitable ointment base.

IDENTIFICATION

• **A.** The retention time of the betamethasone dipropionate peak from the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay* for *Betamethasone Dipropionate*.

• **B.** The retention time of the calcipotriene peak from the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay* for *Calcipotriene*.

• **C.** The UV spectrum of the betamethasone dipropionate peak from the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay* for *Betamethasone Dipropionate*.

• **D.** The UV spectrum of the calcipotriene peak from the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay* for *Calcipotriene*.

ASSAY

• **Betamethasone Dipropionate**

[Note—Protect solutions containing betamethasone dipropionate and beclomethasone dipropionate from light.]

Mobile phase: Acetonitrile and water (50:55)

Diluent: Acetonitrile and water (60:25)

Internal standard solution: 0.4 mg/mL of USP Beclomethasone Dipropionate RS in *Diluent*

Standard stock solution: 0.87 mg/mL of USP Betamethasone Dipropionate RS in *Diluent*

Standard solution: 0.012 mg/mL of USP Betamethasone Dipropionate RS from the *Standard stock solution* prepared as follows. Dilute 1.0 mL of the *Standard stock solution* with 2.0 mL of *Internal standard solution* followed by 22.0 mL of *Diluent* and 50.0 mL of *Mobile phase*.

Sample solution: Nominally 0.012 mg/mL of betamethasone dipropionate from Ointment prepared as follows. Suspend 0.675 g of Ointment in 25 mL of *n*-heptane by heating on a steam bath until the Ointment melts. Add 1.0 mL of *Internal standard solution* and 11.5 mL of *Diluent* and shake for 15 min. Add 25 mL of *Mobile phase* and clear by centrifugation, if necessary, using glass centrifuge tubes. Use the clear lower layer.

Chromatographic system

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

Mode: LC

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

Column: 4-mm × 7.5-cm; 4-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: NLT 1.5 times the retention time of betamethasone dipropionate

System suitability

Samples: *Standard solution* and *Sample solution*

[Note—The relative retention times for calcipotriene, betamethasone dipropionate, and beclomethasone dipropionate are about 0.78, 1.0, and 1.3, respectively.]

Suitability requirements

Resolution: NLT 1.0 between calcipotriene and betamethasone dipropionate; NLT 2.5 between betamethasone dipropionate and beclomethasone dipropionate, *Sample solution*

Tailing factor: 0.8–1.4 for betamethasone dipropionate, *Sample solution*

Relative standard deviation: NMT 2.0% for the peak height ratio of betamethasone dipropionate to beclomethasone dipropionate, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of betamethasone dipropionate ($C_{28}H_{37}FO_7$) in the portion of Ointment taken:

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

R_U = peak height ratio of betamethasone dipropionate to beclomethasone dipropionate from the *Sample solution*

R_S = peak height ratio of betamethasone dipropionate to beclomethasone dipropionate from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

- **Calcipotriene**

[Note—Protect solutions containing calcipotriene from light.]

Solution A: 1.32 g/L of dibasic ammonium phosphate in water

Buffer: *Solution A*, adjusted with 1 M phosphoric acid TS to a pH of 6.0

Mobile phase: Acetonitrile, methanol, and *Buffer* (20:50:30)

Diluent: Methanol and *Solution A* (70:30)

Internal standard solution: 0.1 mg/mL of USP Methyltestosterone RS in *Diluent*

System suitability solution: 0.0025 mg/mL each of USP Calcipotriene RS and USP Calcipotriene Related Compound C RS in acetonitrile, methanol, and *Solution A* (20:50:30)

Standard stock solution: 0.05 mg/mL of USP Calcipotriene RS in *Diluent*

Standard solution: 0.0025 mg/mL of USP Calcipotriene RS from the *Standard stock solution* prepared as follows. Dilute 1.0 mL of the *Standard stock solution* with 1.0 mL of *Internal standard solution* followed by 18.0 mL of *Diluent*. Transfer a portion to a glass test tube with a screw cap and heat at 50° for 15–18 h. Cool to room temperature in a water bath. Prepare this solution simultaneously with the *Sample solution*.

Sample solution: Nominally 0.0025 mg/mL of calcipotriene from Ointment prepared as follows. Suspend 1.0 g of Ointment in 10 mL of *n*-heptane by heating on a steam bath until the Ointment melts. Add 1.0 mL of *Internal standard solution* and 19.0 mL of *Diluent* and shake for 30 min. If necessary, clear the lower layer by centrifugation using glass centrifuge tubes. Transfer a portion of the lower layer to a glass test tube with a screw cap and heat at 50° for 15–18 h. Cool to room temperature in a water bath. Prepare this solution simultaneously with the *Standard solution*.

Chromatographic system

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

Mode: LC

Detector: UV 264 nm. For *Identification D*, use a diode array detector in the range of 200–400 nm.

Column: 4-mm × 12.5-cm; 5-µm packing L1

Flow rate: 2 mL/min

Injection volume: 50 µL

Run time: NLT 1.2 times the retention time of calcipotriene

System suitability

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

[Note—The relative retention times for calcipotriene related compound C and calcipotriene are about 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.0 between calcipotriene and calcipotriene related compound C, *System suitability solution*

Tailing factor: 0.8–1.4 for calcipotriene, *Sample solution*

Relative standard deviation: NMT 2.0% for the peak height ratio of calcipotriene to methyltestosterone, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

[Note—The relative retention times for betamethasone 17-propionate, betamethasone 21-propionate, methyl testosterone, betamethasone dipropionate, and calcipotriene (plus pre-calcipotriene) are about 0.28, 0.28, 0.38, 0.52, and 1.0, respectively. The controlled isomerization of calcipotriene is carried out at 50° producing a mixture of calcipotriene and the isomer (pre-calcipotriene), which is eluted as a single peak.]

Calculate the percentage of the labeled amount of calcipotriene ($C_{27}H_{40}O_3$) in the portion of Ointment taken:

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

R_U = peak height ratio of calcipotriene (plus pre-calcipotriene) to methyltestosterone from the *Sample solution*

R_S = peak height ratio of calcipotriene (plus pre-calcipotriene) to methyltestosterone 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%–114.0%

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