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Clotrimazole and Betamethasone Dipropionate Cream

DEFINITION

Clotrimazole and Betamethasone Dipropionate Cream contains NLT 90.0% and NMT 110.0% of the labeled amount of clotrimazole ($C_{22}H_{17}ClN_2$) and an amount of betamethasone dipropionate equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of betamethasone ($C_{22}H_{29}FO_5$), in a suitable cream base.

IDENTIFICATION

• **A.** The retention times of the major peaks for clotrimazole and betamethasone dipropionate of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay* for clotrimazole and betamethasone.

ASSAY

• **Procedure**

Buffer: 6.6 g/L of dibasic ammonium phosphate in water

Mobile phase: Prepare a mixture of methanol and *Buffer* (7:3), and adjust with phosphoric acid to a pH of 7.0 ± 0.2. Pass through a membrane filter having a 0.45-µm or finer pore size, and degas.

Internal standard solution: 0.15 mg/mL of progesterone in alcohol

Clotrimazole stock solution: 5 mg/mL of USP Clotrimazole RS in alcohol

Betamethasone dipropionate stock solution: 6.4*J* mg/mL of USP Betamethasone Dipropionate RS in alcohol, *J* being the ratio of the labeled amount of betamethasone (in mg/g) to the labeled amount of clotrimazole (in mg/g) in the Cream

Clotrimazole related compound A stock solution: 0.5 mg/mL of USP Clotrimazole Related Compound A RS in methanol

Standard solution: Transfer 1.0 mL of *Clotrimazole related compound A stock solution* to a suitable container, and evaporate to dryness in a water bath at room temperature under a stream of nitrogen. To the residue add 2.0 mL each of *Clotrimazole stock solution*, *Betamethasone dipropionate stock solution*, and *Internal standard solution*.

Sample solution: Weigh a portion of Cream equivalent to 10 mg of clotrimazole, and transfer to a screw-capped, 50-mL centrifuge tube. Add 2.0 mL of *Internal standard solution* and 4.0 mL of alcohol, place the cap on the tube, and heat at 60° in a water bath for 10 min, with occasional shaking. Remove the tube from the bath, cool in an ice bath for 20 min, and promptly centrifuge. Transfer a portion of the supernatant to a test tube, and use as the *Sample solution*.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 10-µm packing L1

Flow rate: 1.7 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times for betamethasone dipropionate, clotrimazole related compound A, progesterone, and clotrimazole are about 1.0, 1.2, 1.4, and 1.7, respectively.]

Suitability requirements

Resolution: NLT 1.0 between betamethasone dipropionate and clotrimazole related compound A, NLT 1.5 between clotrimazole related compound A and progesterone, and NLT 1.8 between progesterone and clotrimazole

Relative standard deviation: NMT 2.0% determined from clotrimazole and betamethasone dipropionate and NMT 4.0% determined from clotrimazole related compound A

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of clotrimazole ($C_{22}H_{17}ClN_2$) in the portion of Cream taken:

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

R_U = peak response ratio of clotrimazole to progesterone from the *Sample solution*

R_S = peak response ratio of clotrimazole to progesterone from the *Standard solution*

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

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

Calculate the percentage of the labeled amount of betamethasone ($C_{22}H_{29}FO_5$) in the portion of Cream taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

R_U = peak response ratio of betamethasone dipropionate to progesterone from the *Sample solution*

R_S = peak response ratio of betamethasone dipropionate to progesterone from the *Standard solution*

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

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

M_{r1} = molecular weight of betamethasone, 392.46

M_{r2} = molecular weight of betamethasone dipropionate, 504.60

Acceptance criteria: 90.0%–110.0% of the labeled amount of clotrimazole ($C_{22}H_{17}ClN_2$); 90.0%–110.0% of the labeled amount of betamethasone ($C_{22}H_{29}FO_5$)

IMPURITIES

• **Organic Impurities: Limit of Clotrimazole Related Compound A**

Buffer, Mobile phase, Internal standard solution, Clotrimazole stock solution, Betamethasone dipropionate stock solution, Clotrimazole related compound A stock solution, Standard solution, Sample solution, Chromatographic system, and **System suitability:** Use as directed in the *Assay*.

Analysis: Using the chromatograms of the *Standard solution* and *Sample solution* as obtained in the *Assay*, calculate the percentage of clotrimazole related compound A in the portion of Cream taken:

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

R_U = peak response ratio of clotrimazole related compound A to progesterone from the *Sample solution*

R_S = peak response ratio of clotrimazole related compound A to progesterone from the *Standard solution*

C_S = concentration of USP Clotrimazole Related Compound A RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: NMT 5.0%

PERFORMANCE TESTS

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

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** It meets the requirements for the absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in collapsible tubes or tight containers.

• **USP Reference Standards ⟨11⟩**

USP Betamethasone Dipropionate RS

USP Clotrimazole RS

USP Clotrimazole Related Compound A RS

(*o*-Chlorophenyl)diphenylmethanol.

$C_{19}H_{15}ClO$ 294.78

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