Edition: BP 2025 (Ph. Eur. 11.6 update)

Fluocinolone Cream

General Notices

Action and use

Glucocorticoid.

DEFINITION

Fluocinolone Cream contains Fluocinolone Acetonide or Fluocinolone Acetonide Dihydrate in a suitable basis.

The cream complies with the requirements stated under Topical Semi-solid Preparations and with the following requirements.

Content of fluocinolone acetonide, $C_{24}H_{30}F_2O_6$

90.0 to 110.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Disperse, by shaking, a quantity of the preparation being examined containing 0.25 mg of Fluocinolone Acetonide in 2 mL of *chloroform*, add 10 mL of *methanol*, shake vigorously, cool in ice for 15 minutes, centrifuge at 3000 revolutions per minute for 15 minutes, decant the clear, supernatant liquid, evaporate to dryness on a water bath in a current of nitrogen and dissolve the residue in 1 mL of *chloroform*.
(2) 0.025% w/v solution of *fluocinolone acetonide BPCRS* in *chloroform*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel G*.
(b) Use the mobile phase as described below.
(c) Apply 5 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air until the solvent has evaporated, heat at 105° for 5 minutes and spray whilst hot with *alkaline tetrazolium blue solution*.

MOBILE PHASE

1 volume of *triethylamine*, 10 volumes of *methanol*, 40 volumes of *chloroform* and 60 volumes of n-*hexane*.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

B. In the Assay, the chromatogram obtained with solution (2) shows a peak with the same retention time as the peak due to fluocinolone acetonide in the chromatogram obtained with solution (1).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

For creams containing 0.025% to 0.2% w/w of fluocinolone acetonide

(1) 0.025% w/v of *fluocinolone acetonide BPCRS* and 0.005% w/v of *phenacetin* (internal standard) in *chloroform*.
(2) To a quantity of the cream containing 2.5 mg of Fluocinolone Acetonide add 60 mL of a solution prepared by adding 80 mL of *methanol* to 20 mL of a 25% w/v solution of *lithium chloride* and disperse by shaking vigorously. Add 100 mL of *cyclohexane*, shake gently for 2 minutes and separate the lower, aqueous methanolic layer, taking care to exclude any solid matter that separates at the interface. Repeat the extraction using a further 25 mL of the lithium chloride solution. To the combined extracts add a solution of 11 g of *aluminium potassium sulfate* in 214 mL of *water* followed by 50 mL of *chloroform*, shake vigorously for about 3 minutes, allow the layers to separate and filter the chloroform extract through filter paper (Whatman No. 1 is suitable), previously moistened with *chloroform*, again excluding any solid matter at the interface. Repeat the extraction with 50- and 10-mL quantities of *chloroform*, filtering the extracts as before. Evaporate the combined extracts to dryness on a water bath in a current of nitrogen, dissolve the residue in 5 mL of *chloroform*, transfer to a 10-mL graduated flask with the aid of *chloroform* and add sufficient *chloroform* to produce 10 mL.
(3) Prepare in the same manner as solution (2) but add 1.0 mL of a 0.050% w/v solution of *phenacetin* to the *chloroform* solution before dilution to 10 mL.

For creams containing 0.01% w/w of fluocinolone acetonide

(1) 0.01% w/v of *fluocinolone acetonide BPCRS* and 0.002% w/v of *phenacetin* (internal standard) in *chloroform*.
(2) Prepare as described above but using a quantity of the cream containing 1 mg of Fluocinolone Acetonide.
(3) Prepare in the same manner as solution (2) but add 1 mL of a 0.02% w/v solution of *phenacetin* to the *chloroform* solution before diluting to 10 mL.

For creams containing 0.00625% w/w of fluocinolone acetonide

(1) 0.00625% w/v of *fluocinolone acetonide BPCRS* and 0.00125% w/v of *phenacetin* (internal standard) in *chloroform*.
(2) Prepare as described above but using a quantity of the cream containing 0.62 mg of Fluocinolone Acetonide.
(3) Prepare in the same manner as solution (2) but add 1 mL of a 0.0125% w/v solution of *phenacetin* to the *chloroform* solution before diluting to 10 mL.

For creams containing 0.0025% w/w of fluocinolone acetonide

(1) 0.0025% w/v of *fluocinolone acetonide BPCRS* and 0.0005% w/v of *phenacetin* (internal standard) in *chloroform*.
(2) Prepare as described above but using a quantity of the cream containing 0.25 mg of Fluocinolone Acetonide.
(3) Prepare in the same manner as solution (2) but add 1 mL of a 0.005% w/v solution of *phenacetin* to the *chloroform* solution before diluting to 10 mL.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (20 cm × 5 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Spherisorb ODS 1 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.8 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 243 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

58 volumes of *hexane*, 40 volumes of *chloroform*, 2 volumes of *methanol* and 0.1 volume of *glacial acetic acid*.

SYSTEM SUITABILITY

The assay is not valid unless the *resolution factor* (R_s) between the peaks due to fluocinolone acetonide and phenacetin is more than 2, and the *capacity factors* (*k′*) of fluocinolone acetonide and phenacetin are about 3 and 2, respectively. If these conditions are not achieved, adjust the concentration of *methanol* in the mobile phase, increasing its concentration to reduce the value of *k′* and reducing its concentration to increase the value of *k′*. If the correct values cannot be obtained by this means, the column is faulty and must be repacked. If, when the correct *k′* values have been obtained, the value of

R_s is less than 2, reduce the concentration of *chloroform* in the mobile phase by 5% to obtain an increased retention time for both fluocinolone acetonide and phenacetin and re-adjust the *k'* values to the specified values by increasing the concentration of *methanol*. Repeat the adjustment of chloroform and methanol concentrations until correct values for both R_s and *k'* have been obtained.

DETERMINATION OF CONTENT

Calculate the content of $C_{24}H_{30}F_2O_6$ in the cream using the declared content of $C_{24}H_{30}F_2O_6$ in *fluocinolone acetonide BPCRS*.

LABELLING

When the active ingredient is Fluocinolone Acetonide Dihydrate, the quantity is stated in terms of the equivalent amount of fluocinolone acetonide.