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Calcipotriol Scalp Application

General Notices

Action and use

Vitamin D analogue.

DEFINITION

Calcipotriol Scalp Application contains either Calcipotriol or Calcipotriol Monohydrate in a suitable basis.

The scalp application complies with the requirements stated under Liquids For Cutaneous Application and with the following requirements.

Content of calcipotriol, $C_{27}H_{40}O_3$

90.0 to 110.0% of the stated amount.

A reversible isomerisation to pre-calcipotriol takes place in solution, depending on temperature and time. The activity is due to both compounds.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, protected from light, using the following solutions.
Solvent A

1 volume of *triethylamine* and 9 volumes of *dichloromethane*.
(1) Evaporate a quantity of the scalp application containing the equivalent of 0.5 mg of calcipotriol to dryness at a temperature not exceeding 30° and dissolve the residue in 1 mL of solvent A.
(2) 0.05% w/v of *calcipotriol monohydrate EPCRS* in solvent A.
(3) Place 2 mg of *calcipotriol monohydrate EPCRS* in a vial and dissolve in 200 µL of solvent A. Close the vial and keep it in a water bath at 60° for 2 hours (generation of pre-calcipotriol).

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel F_{254}*.
(b) Use the mobile phase as described below.
(c) Apply 50 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air and then heat at 140° for 10 minutes. Whilst hot, spray the plate with an *alcoholic solution of sulfuric acid*, dry at 140° for not more than 1 minute and examine in *ultraviolet light (365 nm)*.

MOBILE PHASE

20 volumes of *2-methylpropanol* and 80 volumes of *dichloromethane*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) shows two clearly separated spots.

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CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds in position and colour to that in the chromatogram obtained with solution (2). A secondary spot in the chromatogram obtained with solution (1) corresponds in position and colour to the pre-calcipotriol spot in solution (3).

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

TESTS

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, protected from light, using the following solutions prepared in solvent B.

Solvent B 30 volumes of 0.01M *ammonium phosphate* and 70 volumes of *methanol*.

(1) Evaporate a quantity of the scalp application containing the equivalent of 0.5 mg of calcipotriol to dryness at a temperature not exceeding 30° and dissolve the residue in 4 mL.
(2) Dilute 0.1 mL of solution (1) to 10 mL.
(3) 0.004% w/v of *calcipotriol monohydrate EPCRS*.
(4) Dilute 1 volume of solution (2) to 10 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.0 mm) packed with *octadecylsilyl silica gel for chromatography* (3 µm) (Luna C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 264 nm.
(f) Inject 50 µL of each solution.
(g) For solution (1), allow the chromatography to proceed for 2 times the retention time of calcipotriol.

MOBILE PHASE

30 volumes of *water* and 70 volumes of *methanol*.

When the chromatograms are recorded under the prescribed conditions the retention times relative to calcipotriol (retention time, about 13.5 minutes) are: pre-calcipotriol, about 0.86; impurity C, about 0.92 and impurity D, about 1.3.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *peak-to-valley ratio* between calcipotriol and impurity C is at least 5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity C is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%);

the area of any peak corresponding to impurity D is not greater than 3.5 times the area of the principal peak in the chromatogram obtained with solution (2) (3.5%);

the area of any other *secondary peak* is not greater than twice the area of the principal peak in the chromatogram obtained with solution (4) (0.2%);

the sum of the areas of any other *secondary peak* is not greater than half the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

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Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, protected from light, using the following solutions prepared in solvent B, as described under Related substances.

(1) Dilute a weight of the scalp application containing the equivalent of 0.35 mg of calcipotriol to 10 mL.
(2) 0.0037% w/v of *calcipotriol monohydrate EPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the *peak-to-valley ratio* between calcipotriol and impurity C is at least 5.

DETERMINATION OF CONTENT

Calculate the content of $C_{27}H_{40}O_3$ in the scalp application using the combined areas of the peaks due to calcipotriol and pre-calcipotriol in the chromatograms obtained with solutions (1) and (2) and the declared content of $C_{27}H_{40}O_3$ in *calcipotriol monohydrate EPCRS*.

STORAGE

Calcipotriol Scalp Solution should be protected from light.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of calcipotriol.

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