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

Adapalene Cream

General Notices

Action and use

Vitamin A analogue (retinoid); treatment of acne.

DEFINITION

Adapalene Cream contains Adapalene in a suitable basis.

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

Content of adapalene, $C_{28}H_{28}O_3$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Add 10 mL of *stabiliser-free tetrahydrofuran* to a quantity of cream containing 5 mg of Adapalene and shake to disperse. Add sufficient *methanol* to produce a solution containing 0.025% w/v of Adapalene and filter (a 0.2-µm Dynagard PP filter is suitable).
(2) 0.025% w/v of *adapalene BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *octadecylsilyl silica gel F_{254}* (Merck silica gel 60 RP-18 F_{254} plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 1 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate dry in air and examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

18 volumes of *stabiliser-free tetrahydrofuran* and 82 volumes of *methanol*.

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).

B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the principal peak in the chromatogram obtained with solution (2).

TESTS

Acidity

pH, 4.5 to 5.5, Appendix V L.

Related substances

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

Solvent A 2 volumes of *trifluoroacetic acid* and 100 volumes of *water*.

Solvent B 10 volumes of solvent A, 25 volumes of *acetonitrile*, 30 volumes of *propan-2-ol* and 35 volumes of *stabiliser-free tetrahydrofuran*.

(1) To a quantity of the cream containing 1 mg of Adapalene, add 7 mL of *stabiliser-free tetrahydrofuran* and mix with the aid of ultrasound. Add 6 mL of *propan-2-ol*, shake, add 2 mL of solvent A and dilute to 20 mL with *acetonitrile*.
(2) Dilute 1 volume of solution (1) to 100 volumes with solvent B.
(3) 0.005% w/v of *adapalene impurity standard BPCRS* in a mixture of equal volumes of *stabiliser-free tetrahydrofuran* and *water*.
(4) Dilute 1 volume of solution (2) to 20 volumes with solvent B.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (LiChrospher 100 RP 18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use an ambient column temperature.
(e) Use a fluorimetric detector with the following programme.

Time (Minutes)	Excitation wavelength (nm)	Emission wavelength (nm)
0 - 11	260	380
11 - 30	260	347

(f) Inject 10 µL of each solution.

MOBILE PHASE

Mobile phase A 0.2 volume of *trifluoroacetic acid* and 100 volumes of *water*.

Mobile phase B 40 volumes *stabiliser-free tetrahydrofuran* and 60 volumes of *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-3	40→17	60→83	linear gradient
3-30	17	83	isocratic
30-31	17→40	83→60	linear gradient
31-40	40	60	re-equilibration

When the chromatograms are recorded under the prescribed conditions the retention times relative to adapalene (retention time about 6.5 minutes) are: impurity A, about 0.5 and impurity D, about 3.1.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) resembles the chromatogram provided with *adapalene impurity standard BPCRS*.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak due to impurity A or impurity D is not greater than the area of the corresponding peak in the chromatogram obtained with solution (3) (0.5%);

the area of any other *secondary peak* is not greater than 0.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the sum of the impurities is not greater than 1.0%.

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.05%).

ASSAY

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

Solvent C 21 volumes of *water*, 36 volumes of *stabiliser-free tetrahydrofuran* and 43 volumes of *acetonitrile*.

(1) Disperse a quantity of the cream containing 1 mg of Adapalene in 10 mL of *stabiliser-free tetrahydrofuran* and shake with the aid of ultrasound for 5 minutes, dilute to 50 mL with solvent C and filter (a 0.2-µm Dynagard filter is suitable).
(2) Dilute 1 volume of a 0.01% w/v of *adapalene BPCRS* in *stabiliser-free tetrahydrofuran* to 5 volumes with solvent C.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4 mm) with a stainless steel pre-column (4 mm × 4 mm) both packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (LiChrospher 100 RP 18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 270 nm.
(f) Inject 25 µL of each solution.

MOBILE PHASE

0.02 volume of *trifluoroacetic acid*, 21 volumes of *water*, 36 volumes of *stabiliser-free tetrahydrofuran* and 43 volumes of *acetonitrile*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the *column efficiency*, determined on the peak due to adapalene, is at least 4500 *theoretical plates* per metre.

DETERMINATION OF CONTENT

Calculate the content of $C_{28}H_{28}O_3$ in the cream using the declared content of $C_{28}H_{28}O_3$ in *adapalene BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A and D listed under Adapalene.