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

Acitretin Capsules

General Notices

Action and use

Vitamin A analogue (retinoid); treatment of psoriasis; ichthyosis; Darier's disease.

DEFINITION

Acitretin Capsules contain Acitretin.

The capsules comply with the requirements stated under Capsules and with the following requirements.

Carry out the following tests avoiding exposure to actinic light and using freshly prepared solutions.

Content of acitretin, $C_{21}H_{26}O_3$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Dissolve a quantity of the capsule contents containing 25 mg of Acitretin with sufficient *methanol* to produce 250 mL, filter and dilute 1 volume of the filtrate to 20 volumes with *methanol*. The *light absorption* spectra, Appendix II B, in the range 300 nm to 400 nm is concordant with a 0.0005% w/v solution of *acitretin BPCRS* in *methanol*.
B. In the Assay, the chromatogram obtained with solution (1) shows a peak with the same retention time as the principal peak in the chromatogram obtained with solution (2).

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 1, rotating the basket at 100 revolutions per minute.
(b) Use 900 mL of a 3% w/v solution of *sodium lauryl sulfate* adjusted to pH 9.5 with 0.01M *hydrochloric acid* or 0.01M *sodium hydroxide*, at a temperature of 37°, as the medium.

PROCEDURE

After 45 minutes withdraw a sample of the medium, filter through a 10-µm filter and measure the *absorbance* of the filtrate, suitably diluted with sufficient dissolution medium to give a solution expected to contain about 0.0005% w/v of Acitretin, at the maximum at about 348 nm, Appendix II B, using dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of acitretin, $C_{21}H_{26}O_3$, in the medium taking 1373 as the value of A(1%, 1 cm) at the maximum at 348 nm.

LIMITS

The amount of Acitretin released is not less than 75% (Q) of the stated amount.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in a mixture of 10 volumes of *tetrahydrofuran* and 13 volumes of *methanol* (solvent A).

(1) Shake a quantity of the capsule contents containing 25 mg of Acitretin with 8 mL of *water* in a water bath at 45° for 10 minutes. Mix with the aid of ultrasound for 15 minutes, add sufficient solvent A to produce 100 mL and mix with the aid of ultrasound for a further 5 minutes. Filter through a 0.45-µm filter (PTFE is suitable).
(2) Dilute 1 volume of solution (1) to 100 volumes with solvent A. Further dilute 4 volumes of this solution to 10 volumes with solvent A.
(3) 0.00025% w/v each of *tretinoin EPCRS* and *acitretin BPCRS* in solvent A.
(4) Dilute 1 volume of solution (2) to 4 volumes with solvent A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Spherisorb ODS 2 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 365 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

0.5 volume of *glacial acetic acid*, 5 volumes of *absolute ethanol*, 21 volumes of *water* and 74 volumes of *methanol*.

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (3), the *resolution* between the peaks due to acitretin and tretinoin is at least 3.0;

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.4%);

the area of not more than one *secondary peak* is greater than half the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of all the *secondary peaks* is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (1%).

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, using the following solutions in a mixture of 10 volumes of *tetrahydrofuran* and 13 volumes of *methanol* (solvent A).

(1) Shake a quantity of the mixed contents of 20 capsules containing 25 mg of Acitretin with 8 mL of *water* in a water bath at 45° for 10 minutes. Mix with the aid of ultrasound for 15 minutes, add sufficient solvent A to produce 100 mL and mix with the aid of ultrasound for a further 5 minutes. Filter through a 0.45-µm filter (PTFE is suitable) and dilute 5 mL of the filtrate to 25 mL with solvent A.
(2) 0.005% w/v of *acitretin BPCRS* in solvent A.
(3) 0.00025% w/v each of *acitretin BPCRS* and *tretinoin EPCRS* in solvent A.

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 (3), the *resolution* between the peaks due to tretinoin and acitretin is at least 3.0.

DETERMINATION OF CONTENT

Calculate the content of acitretin, $C_{21}H_{26}O_3$, in the capsules using the declared content of $C_{21}H_{26}O_3$ in *acitretin BPCRS*.

STORAGE

Acitretin Capsules should be protected from light.