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

Aciclovir Cream

General Notices

Action and use

Purine nucleoside analogue; antiviral (herpesviruses).

DEFINITION

Aciclovir Cream contains Aciclovir in a suitable basis.

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

Content of aciclovir, $C_8H_{11}N_5O_3$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Shake a quantity of the well-mixed cream containing about 7.5 mg of Aciclovir with 50 mL of 0.5M *sulfuric acid*. Shake well with 50 mL of *ethyl acetate*, allow to separate and collect the clear lower aqueous layer. Wash the organic layer with 20 mL of 0.5M *sulfuric acid* and dilute the combined washings and the aqueous layer to 100 mL with 0.5M *sulfuric acid*. Mix well and filter (Whatman GF/F is suitable). Discard the first few mL of the filtrate and to 10 mL of the filtrate add sufficient *water* to produce 50 mL. The *light absorption*, Appendix II B, in the range 230 to 350 nm of the solution exhibits a maximum at 255 nm and a broad shoulder at about 274 nm.
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 due to aciclovir in the chromatogram obtained with solution (2).

TESTS

Related substances

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

Solution A: 1 volume of *dimethyl sulfoxide* and 4 volumes of *water*.

(1) Mix with the aid of ultrasound a quantity of the well-mixed cream containing 25 mg of Aciclovir in 10 mL of *dimethyl sulfoxide*, dilute to 25 mL with solution A and filter through a 0.2-µm nylon filter.
(2) Dilute 1 volume of solution (1) to 100 volumes with solution A and dilute 1 volume of this solution to 5 volumes with solution A.
(3) Dissolve 5 mg of *aciclovir for system suitability A EPCRS* in 1 mL of *dimethyl sulfoxide* and dilute to 5 mL with *water*.
(4) Dissolve the contents of a vial of *aciclovir for impurity C identification EPCRS* in 200 µL of *dimethyl sulfoxide* and dilute to 1 mL with *water*. Prepare the solution immediately before use.
(5) Dissolve the contents of a vial of *aciclovir for impurity G identification EPCRS* in 1 mL of solution (3).

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Supelcosil LC-18-DB is suitable).
(b) Use gradient 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 254 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

Phosphate buffer solution pH 3.1 Dissolve 3.48 g of *dipotassium hydrogen orthophosphate* in 1000 mL of *water* and adjust to pH 3.1 with *orthophosphoric acid*.

Phosphate buffer solution pH 2.5 Dissolve 3.48 g of *dipotassium hydrogen orthophosphate* in 1000 mL of *water* and adjust to pH 2.5 with *orthophosphoric acid*.

Mobile phase A 1 volume of *acetonitrile* and 99 volumes of phosphate buffer solution pH 3.1.

Mobile phase B 50 volumes of *acetonitrile* and 50 volumes of phosphate buffer solution pH 2.5.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-5	100	0	isocratic
5-27	100→80	0→20	linear gradient
27-40	80	20	isocratic
40-46	80→100	20→0	linear gradient

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (4), the *resolution* between the peaks due to impurity C and aciclovir is at least 1.5.

in the chromatogram obtained with solution (5), the *resolution* between the peaks due to impurity K and impurity G is at least 1.5.

LIMITS

Identify any peak in solution (1) corresponding to impurity C using the chromatogram obtained with solution (4) and multiply the area of this peak by a correction factor of 2.2.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity B is not greater than 5 times the area of the principal peak in the chromatogram obtained with solution (2) (1.0%);

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

the sum of the areas of any *secondary peaks* is not greater than 10 times the area of the principal peak in the chromatogram obtained with solution (2) (2.0%).

Disregard any peak with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

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

Solution A: 1 volume of *dimethyl sulfoxide* and 4 volumes of *water*.

(1) Mix with the aid of ultrasound a quantity of the well-mixed cream containing 25 mg of Aciclovir in 10 mL of *dimethyl sulfoxide*, dilute to 25 mL with solution A and filter through a 0.2-µm nylon filter. Further dilute 1 volume to 10 volumes with solution A.
(2) Dissolve 25 mg of *aciclovir BPCRS* in 10 mL of *dimethyl sulfoxide*. Dilute 2 volumes to 5 volumes with solution A and dilute 1 volume of this solution to 10 volumes with solution A.
(3) Dissolve the contents of a vial of *aciclovir for impurity C identification EPCRS* in 200 µL of *dimethyl sulfoxide* and dilute to 1 mL with *water*. Prepare the solution immediately before use.

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 factor* between the peaks due to impurity C and aciclovir is at least 1.5.

DETERMINATION OF CONTENT

Calculate the content of $C_8H_{11}N_5O_3$ in the cream using the declared content of $C_8H_{11}N_5O_3$ in *aciclovir BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Aciclovir.