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Aciclovir Oral Suspension

General Notices

Action and use

Purine nucleoside analogue; antiviral (herpesviruses).

DEFINITION

Aciclovir Oral Suspension is a suspension of Aciclovir in a suitable flavoured vehicle.

The oral suspension complies with the requirements stated under Oral Liquids 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. The *light absorption*, Appendix II B, in the range 230 to 250 nm of the solution prepared in the Assay before the final dilution exhibits a maximum at 255 nm and a broad shoulder at about 274 nm.
B. In the Related substances test, 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 a solution prepared as follows. Dissolve 25 mg of *aciclovir BPCRS* in 10 mL of *dimethyl sulfoxide* and dilute 2 volumes of the resulting solution to 5 volumes with the solvent mixture used in the Related substances test.

TESTS

Acidity

pH, 4.0 to 7.0, Appendix V L.

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) To a quantity of the oral suspension containing 0.5 g of Aciclovir add 20 mL of *dimethyl sulfoxide*, shake to disperse and add sufficient solvent mixture to produce 100 mL and filter through a 0.2-µm nylon filter. Dilute 1 volume of the filtrate to 5 volumes with solution A.
(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 0.25 times the area of the principal peak in the chromatogram obtained with solution (2) (0.05%).

ASSAY

To a weighed quantity containing 0.4 g of Aciclovir add 400 mL of *water* and 25 mL of 1M *sulfuric acid*, shake well, disperse with the aid of ultrasound for 10 minutes and add sufficient *water* to produce 500 mL. Filter the resulting solution, discard

the first few mL of filtrate and dilute 5 mL of the filtrate to 200 mL with 0.05M *sulfuric acid*. Add 10 mL of the resulting solution to 5 mL of a 0.01% w/v solution of *cetrimide* in 0.05M *sulfuric acid*, add sufficient 0.05M *sulfuric acid* to produce 100 mL and measure the *fluorescence,* Appendix II E, using an excitation wavelength of 308 nm and an emission wavelength of 415 nm. Set the instrument to zero using a 0.0005% w/v solution of *cetrimide* in 0.05M *sulfuric acid*. Calculate the content of $C_8H_{11}N_5O_3$ in the oral suspension from the *fluorescence* obtained by carrying out the operation at the same time using a mixture prepared by adding 10 mL of a 0.002% w/v solution of *aciclovir BPCRS* in 0.05M *sulfuric acid* and beginning at the words '… to 5 mL of a 0.01% w/v solution of *cetrimide* ...'. Determine the *weight per mL* of the oral suspension, Appendix V G, and calculate the content of $C_8H_{11}N_5O_3$, weight in volume, 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.