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Aciclovir Infusion

General Notices

Aciclovir Intravenous Infusion

Action and use

Purine nucleoside analogue; antiviral (herpesviruses).

DEFINITION

Aciclovir Infusion is a sterile solution containing aciclovir sodium. It is prepared by dissolving Aciclovir Sodium for Infusion with a suitable diluent in accordance with the manufacturer's instructions.

The infusion complies with the requirements stated under Parenteral Preparations and with the following requirements.

TESTS

Bacterial endotoxins

Carry out the test for *bacterial endotoxins*, Appendix XIV C. The endotoxin limit concentration of the infusion, diluted, if necessary, with *water BET* to give a solution containing the equivalent of 25 mg of Aciclovir per mL is 4.37 IU per mL.

STORAGE

Aciclovir Infusion should be used within the period recommended by the manufacturer when prepared and stored strictly in accordance with the manufacturer's instructions.

LABELLING

The strength is stated in terms of the equivalent amount of Aciclovir in a suitable dose-volume.

ACICLOVIR SODIUM FOR INFUSION

DEFINITION

Aciclovir Sodium for Infusion is a sterile material prepared from Aciclovir with the aid of a suitable alkali. It may contain excipients. It is supplied in a sealed container.

The contents of the sealed container comply with the requirements for Powders for Injections or Infusions stated under Parenteral 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. Dissolve the total contents of 10 containers in sufficient 0.1M *hydrochloric acid* to produce 500 mL. Dilute 3 mL of the resulting solution to 100 mL with 0.1M *hydrochloric acid* and dilute 5 mL of the resulting solution with the same solvent to produce a solution containing the equivalent of 0.0015% w/v of Aciclovir. The *light absorption*, Appendix II B, in the range 230 to 350 nm 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 chromatogram obtained with solution (1) is similar to that of the principal peak due to aciclovir in the chromatogram obtained with solution (2).
C. Yield reaction A characteristic of *sodium salts*, Appendix VI.

TESTS

Alkalinity

Dissolve the contents of a sealed container in sufficient *water for injections* to produce a solution containing the equivalent of 2.5% w/v of Aciclovir (solution A). The pH of solution A is 10.7 to 11.7, Appendix V L.

Clarity and colour of solution

Solution A is not more opalescent than *reference suspension II*, Appendix IV A, and not more intensely coloured than *reference solution* Y_6, Appendix IV B, Method II.

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) Dissolve the contents of a sealed container in sufficient *dimethyl sulfoxide* to produce a solution containing the equivalent of 2.5% w/v of Aciclovir. Dilute 1 volume of the resulting solution to 25 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 (guanine) 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 other *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

Determine the weight of the contents of 10 containers as described in the test for *uniformity of weight*, Appendix XII C1, Powders for Parenteral Use. 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) Shake a quantity of the powder containing the equivalent of 25 mg of Aciclovir in 10 mL of *dimethyl sulfoxide*. Dilute 2 volumes of the filtrate to 5 volumes with solution A and dilute 1 volume of this solution 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* 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 powder 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.

LABELLING

The label of the sealed container states the quantity of aciclovir sodium in terms of the equivalent amount of Aciclovir.