Aciclovir tablets (Acicloviri compressi)

2014-01

Category: Antiviral (Purine nucleoside analogue).

Storage: Preserve in tightly-closed containers. Protect from light and moisture.

Additional information. Strength in the current WHO Model list of essential medicines: 200 mg. Strengths in the current WHO Model list of essential medicines for children: 200 mg.

Requirements

Complies with the monograph on *Tablets*.

Definition: Aciclovir tablets contain not less than 90.0% and not more than 110.0% of the labelled amount of aciclovir ($C_8H_{11}N_5O_3$).

Identity tests

-Either test A and C or test B and C may be applied.

A. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography using the conditions given under" Guanine and related test", A1. The principal spot in the chromatogram obtained with solution (B) corresponds in position, appearance and intensity to the spot due to aciclovir in the chromatogram obtained with solution (C).

B. Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography using the conditions given under "Assay", test A. The retention time of the principal peak in the chromatogram obtained with solution (1) corresponds to the retention time of the peak due to aciclovir in the chromatogram obtained with the solution (2).

C. The absorption spectrum (*1.6*) of the solution, prepared as described under "Assay", test B, when observed between 230 nm and 350 nm, exhibits one maximum at about 255 nm.

Dissolution

Carry out the test as described under *5.5 Dissolution test for solid oral dosage forms* using as the dissolution medium, 900 mL of Hydrochloric acid (~4 g/L) TS and rotating the paddle at 75 revolutions per minute. At 30 minutes withdraw a sample of 10 mL of the medium through an in-line filter. Measure the absorbance *(1.6)* of the filtered sample, suitably diluted if necessary, at a wavelength of 255 nm. At the same time measure the absorbance of a suitable solution of aciclovir RS in hydrochloric acid (~4 g/L) TS using the same buffer as the blank.

For each of the tablets tested calculate the total amount of aciclovir ($C_8H_{11}N_5O_3$) in the medium from the absorbances obtained using the declared content of $C_8H_{11}N_5O_3$ in aciclovir RS. Use the requirements as described under *5.5 Dissolution test for solid oral dosage forms*, Acceptance criteria to evaluate the results: the amount in solution is not less than 75% (Q) of the amount declared on the label.

Guanine

-Either test A or test B may be applied.

A. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography using cellulose R1 as the coating substance and a mixture of 10 volumes of propan-1-ol, 30 volumes of ammonia (260 g/L) and 60 volumes of ammonium sulfate (50 g/L). Apply separately to the plate 10 µL of each of the following four, freshly prepared solutions in sodium hydroxide (0.1 mol/L) TS. For solution (A) shake a quantity of the powdered tablets, containing about 25 mg of aciclovir, with 5 mL of sodium hydroxide (0.1 mol/L) TS, filter and use the filtrate. For solution (B) dilute 1 volume of (A) to 10 volumes. For solution (C) use a solution of 0.5 mg of aciclovir RS and 0.5 mg of guanine RS per mL. For solution (D) use 50 µg of guanine R per mL. After removing of the plate from the chromatographic chamber allow it to dry exhaustively in air and examine the chromatogram under ultraviolet light (254 nm). In the chromatogram obtained with solution (C) guanine is eluted with a R_f value of 0.5 and aciclovir with a R_f value of 0.7. The test is not valid unless this chromatogram shows two clearly separated spots. Any secondary spot corresponding to guanine in the chromatogram obtained with solution (A) is not more intense than the principal spot in the chromatogram obtained with solution (D) (1.0%).

B. Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography using the conditions given under "Assay", test A.

Prepare the following solutions. For solution (1) shake a quantity of the powdered tablets, containing 25 mg of aciclovir, with 5.0 mL of sodium hydroxide (0.1 mol/L) TS and dilute to 25.0 mL with water, filter and use the

filtrate. For solution (2) dissolve 10 mg of guanine R in 10 mL of sodium hydroxide (0.1 mol/L) TS and dilute to 100.0 mL with water R. Then dilute 5.0 mL of this solution to 50.0 mL with water. For solution (3) dissolve 5 mg of aciclovir RS, 5 mg of guanine R in 10 mL of sodium hydroxide (0.1 mol/L) TS and dilute to 100 mL with water R.

Inject 20 µL of solution (3). The peak of guanine is eluted at a relative retention of about 0.5 with reference to aciclovir (retention time about 10 minutes). The test is not valid unless the resolution between the peak due to aciclovir and the peak due to guanine is at least 3.0.

Inject separately 20 µL each of solutions (1) and (2). In the chromatogram obtained with solution (1) the area of any peak corresponding to guanine is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1.0%).

Assay

-Either test A or test B may be applied.

A. Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography using a stainless steel column (25 cm x 4.6 mm),

packed with particles of silica gel, the surface of which has been modified with chemically-bonded octadecylsilyl group (5 µm).

As the mobile phase, use a mixture of 90 volumes of phosphate buffer, pH 3.1, TS and 10 volumes of acetonitrile R.

Operate with a flow rate of 1.0 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of 254 nm. Maintain the column at 30 °C.

Prepare the following solutions. For solution (1) shake a quantity of the powdered tablets, equivalent to about 20 mg of aciclovir, accurately weighed, with 10 mL of sodium hydroxide (0.1 mol/L) and dilute to 100 mL with water. Dilute 5.0 mL of this solution to 50 mL with water. For solution (2) dissolve 20 mg of aciclovir RS in 10 mL of sodium hydroxide (0.1 mol/L) and dilute to 100 mL with water. Dilute 5.0 mL of this solution to 50 mL with water.

Inject separately 20 µL each of the solutions (1) and (2). Record the chromatograms for about 20 min. The peak of aciclovir is eluted at a retention time of about 10 minutes.

Measure the areas of the peak responses obtained in the chromatograms of solutions (1) and (2) and calculate the percentage content of aciclovir ($C_8H_{11}N_5O_3$) in the tablets using the declared content of $C_8H_{11}N_5O_3$ in aciclovir RS.

B. Weigh and powder 20 tablets. Transfer a quantity of the powder, equivalent to about 0.1 g of Aciclovir, accurately weighed, to a 100 mL volumetric flask, add 60 mL of sodium hydroxide (0.1 mol/L), sonicate for about 15 minutes, allow to cool to room temperature and make up to volume with the same solvent, shake and filter. Transfer 15.0 mL of the filtrate to a 100 mL volumetric flask, add 50 mL of water and 5.8 mL of hydrochloric acid (70 g/L) TS and dilute to volume with water R. Dilute 5.0 mL of the solution to 50.0 mL with hydrochloric acid (0.1 mol/L) TS. Measure the absorbance of the resulting solution in a 1 cm layer at about 255 nm, using hydrochloric acid (0.1 mol/L) TS as the blank. Calculate the percentage content of aciclovir ($C_8H_{11}N_5O_3$) in the tablets using an absorptivity value of 56.0 ($A^{1\%}_{1cm}$ = 560).