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

Valaciclovir Tablets

General Notices

Action and use

Purine nucleoside analogue; antiviral (herpesviruses).

DEFINITION

Valaciclovir Tablets contain Valaciclovir Hydrochloride or Valaciclovir Hydrochloride Hydrate.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of valaciclovir, $C_{13}H_{20}N_6O_4$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the powdered tablets containing the equivalent of 50 mg of valaciclovir with 20 mL of *methanol*, filter (Whatman GF/C is suitable), evaporate the filtrate and dry the residue at 60° for 1 hour. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of Valaciclovir Hydrochloride *(RS 481)*.

TESTS

Dissolution

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

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of *0.1M hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

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

(1) After 45 minutes withdraw a 10-mL sample of the medium and filter using a 0.45-µm filter. Dilute with sufficient *0.1M hydrochloric acid*, if necessary, to contain the equivalent of 0.00278% w/v of valaciclovir.
(2) 0.0031% w/v of *valaciclovir hydrochloride BPCRS* in the dissolution medium.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (5 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm).
(b) Use isocratic elution and the mobile phase described below.

(c) Use a flow rate of 2 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

5 volumes of *acetonitrile* and 95 volumes of 0.1% v/v *orthophosphoric acid* in *water*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the *symmetry factor* is not greater than 2.

DETERMINATION OF CONTENT

Calculate the content of $C_{13}H_{20}N_6O_4$ in the medium using the declared content of $C_{13}H_{20}N_6O_4$ in *valaciclovir hydrochloride BPCRS*.

LIMITS

The amount of valaciclovir 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.

Solvent A 0.1% v/v of *orthophosphoric acid* in *water*.

(1) Shake a quantity of the powdered tablets containing the equivalent of 2.5 g of valaciclovir in 600 mL of 0.1M *hydrochloric acid* with the aid of ultrasound for 10 minutes. Allow to cool and dilute to 1000 mL with 0.1M *hydrochloric acid*. Dilute 4 mL of the resulting solution to 100 mL with solvent A, mix, filter through a 0.45-µm glass fibre filter (Whatman Uniprep is suitable) and use the filtrate.
(2) Dilute 1 volume of solution (1) to 100 volumes.
(3) Dilute 1 volume of solution (2) to 10 volumes.
(4) Mix, with the aid of ultrasound 10 mL of a solution containing 0.004% w/v of *aciclovir BPCRS* in *0.1M hydrochloric acid* with 300 mL of a 0.0166% w/v solution of *valaciclovir hydrochloride BPCRS* in solvent A and dilute to 500 mL with solvent A.
(5) 0.01% w/v of *valaciclovir impurity standard BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.0 mm) packed with *silica gel for chromatography, crown ether* (5 µm) (Diacel Chiral Phase Crownpack CR (+) is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 0.75 mL per minute.
(d) Use a column temperature of 10°.
(e) Use a detection wavelength of 254 nm.
(f) Inject 10 µL of each solution.
(g) Inject solution (1) and continue the chromatography for twice the retention time of valaiciclovir.

MOBILE PHASE

1 volume of *methanol* and 19 volumes of 0.1% v/v *orthophosphoric acid* in *water*.

When the chromatograms are recorded under the prescribed conditions, the retention times relative to valaciclovir (about 4.5 minutes) are: aciclovir, about 0.5; impurity R, about 0.8; impurity I, about 1.5.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (5):

the *symmetry factor* of the peak due to valaciclovir is not greater than 2;

the *resolution* between the peaks due to impurity R and valaciclovir is at least 1.3.

LIMITS

Identify any peak corresponding to aciclovir using the chromatogram obtained with solution (4) and multiply the area of this peak by a correction factor of 0.7.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity R is not greater than 3 times the area of peak due to valaciclovir in the chromatogram obtained with solution (2) (3.0%);

the area of any peak corresponding to aciclovir (impurity B) is not greater than twice the area of the peak due to valaciclovir in the chromatogram obtained with solution (2) (2.0%);

the area of any peak corresponding to impurity I is not greater than half the area of peak due to valaciclovir in the chromatogram obtained with solution (2) (0.5%);

the area of any other *secondary peak* is not greater than the area of the peak due to valaciclovir in the chromatogram obtained with solution (3) (0.1%);

the sum of the areas of any *secondary peaks* is not greater than 5.5 times the area of the peak due to valaciclovir in the chromatogram obtained with solution (2) (5.5%).

Disregard any peak with an area less than 0.5 times the area of the peak due to valaciclovir in the chromatogram obtained with solution (3) (0.05%).

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

Solvent A 0.1% v/v *orthophosphoric acid* in *water*.

(1) Shake a quantity of the powdered tablets containing the equivalent of 2.5 g of valaciclovir in 600 mL of 0.1M *hydrochloric acid* with the aid of ultrasound for 10 minutes. Allow to cool and dilute to 1000 mL with 0.1M *hydrochloric acid*. Dilute 4 mL to 100 mL with solvent A, mix, filter through a 0.45-µm glass fibre filter (Whatman Uniprep is suitable) and use the filtrate.
(2) 0.011% w/v of *valaciclovir hydrochloride BPCRS* in solvent A.
(3) Mix, with the aid of ultrasound 10 mL of a solution containing 0.004% w/v of *aciclovir BPCRS* in *0.1M hydrochloric acid* with 300 mL of a 0.0166% w/v solution of *valaciclovir hydrochloride BPCRS* in solvent A and dilute to 500 mL with solvent A.
(4) 0.01% w/v of *valaciclovir impurity standard BPCRS*.

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 (4):

the *symmetry factor* of the peak due to valaciclovir is not greater than 2;

the *resolution* between the peaks due to impurity R and valaciclovir is at least 1.3.

DETERMINATION OF CONTENT

Calculate the content of $C_{13}H_{20}N_6O_4$ in the tablets using the declared content of $C_{13}H_{20}N_6O_4$ in *valaciclovir hydrochloride BPCRS*.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of valaciclovir.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A, B, I and R listed under Valaciclovir Hydrochloride.