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

Nevirapine Tablets

General Notices

Action and use

Non-nucleoside reverse transcriptase inhibitor; antiviral (HIV).

DEFINITION

Nevirapine Tablets contain Nevirapine.

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

Content of nevirapine, $C_{15}H_{14}N_4O$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the powdered tablets containing 25 mg of Nevirapine with 10 mL of *dichloromethane* and filter through a sintered-glass funnel. Using a glass syringe, pass the filtrate through a 0.45-µm PTFE syringe filter and dry the residue at 105° for 1 hour. Triturate the dried residue with 0.2 g of *potassium bromide*. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of nevirapine (*RS 507*).

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 as the medium 900 mL of a phosphate buffer, at a temperature of 37°, prepared in the following manner. Mix 3.9 mL of *orthophosphoric acid* and 5.73 g of *sodium dihydrogen orthophosphate monohydrate*, and dilute to 1000 mL with *water*. If necessary, adjust the pH to 2.0 using *orthophosphoric acid*.

PROCEDURE

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

(1) After 45 minutes withdraw a sample of the medium and filter (a 0.45-µm Nylon filter is suitable). Use the filtered medium, diluted with the dissolution medium, if necessary, to produce a solution expected to contain 0.0011% w/v of Nevirapine.
(2) 0.054% w/v of *nevirapine BPCRS* in *ethanol (96%)*. Dilute 1 volume to 50 volumes with dissolution medium.
(3) Dissolve the contents of a vial of *nevirapine for peak identification EPCRS* in 2 mL of the dissolution medium.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 3.9 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (4 µm) (Nova-pak C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 214 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

23 volumes of *acetonitrile R1* and 77 volumes of *water R1*.

When the chromatograms are recorded under the prescribed conditions the retention time of nevirapine is about 4 minutes.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity B and nevirapine is at least 3.0.

DETERMINATION OF CONTENT

Calculate the total content of nevirapine, $C_{15}H_{14}N_4O$, in the medium from the chromatograms obtained and using the declared content of $C_{15}H_{14}N_4O$ in *nevirapine BPCRS*.

LIMITS

The amount of nevirapine 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.

(1) Mix with the aid of ultrasound a quantity of the powdered tablets containing 0.2 g of Nevirapine with 40 mL of *acetonitrile* and 20 mL of the mobile phase. Dilute to 200 mL with the mobile phase and filter through a 0.45-µm membrane filter.
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase. Dilute 1 volume of this solution to 5 volumes with the mobile phase.
(3) Dissolve the contents of a vial of *nevirapine for peak identification EPCRS* in 2 mL of the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped amidohexadecylsilyl silica gel for chromatography* (5 µm) (Supelcosil LC-ABZ is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use a column temperature of 35°.
(e) Use a detection wavelength of 220 nm.
(f) Inject 20 µL of each solution.
(g) Allow chromatography to proceed for 4 times the retention time of nevirapine.

MOBILE PHASE

15 volumes of *acetonitrile* and 85 volumes of a 0.288% w/v solution of *ammonium dihydrogen orthophosphate* previously adjusted to pH 5.0 using *dilute sodium hydroxide solution*.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to nevirapine (retention time about 13 minutes) are: impurity B, about 0.7; impurity A, 1.5; impurity C, about 2.8.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity B and nevirapine is at least 3.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *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 all *secondary peaks* is not greater than 3 times the area of the principal peak in the chromatogram obtained with solution (2) (0.6%).

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

ASSAY

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

Solution A: equal volumes of *ethanol* and *water*.

(1) Mix with the aid of ultrasound a quantity of the powdered tablets containing 0.2 g of Nevirapine with 150 mL, and dilute to 200 mL. Mix and centrifuge a portion of the solution. Dilute 1 volume of the supernatant liquid to 50 volumes, filter through a membrane filter (nominal pore size 0.45 µm), and use the filtrate.
(2) 0.002% w/v solution of *nevirapine BPCRS*.
(3) Dissolve the contents of a vial of *nevirapine for peak identification EPCRS* in 2 mL.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution 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 B and nevirapine is at least 3.0.

DETERMINATION OF CONTENT

Calculate the content of nevirapine, $C_{15}H_{14}N_4O$, in the tablets from the chromatograms obtained and using the declared content of $C_{15}H_{14}N_4O_4$ in *nevirapine BPCRS*.

IMPURITIES

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