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Nevirapine Oral Suspension

General Notices

Action and use

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

DEFINITION

Nevirapine Oral Suspension is a suspension of Nevirapine Hemihydrate in a suitable vehicle.

The oral suspension complies with the requirements stated under Oral Liquids and with the following requirements.

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

95.0 to 105.0% of the stated amount.

IDENTIFICATION

In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 190 to 400 nm.

The UV spectrum of the principal peak in the chromatogram obtained with solution (1) is concordant with that of the peak in the chromatogram obtained with solution (2);

the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

TESTS

Dissolution

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

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 25 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.

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

(1) Shake the oral suspension for 30 seconds and place a volume equivalent to one dose into each dissolution vessel. 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 the equivalent of 0.0056% w/v of nevirapine.
(2) 1.4% w/v of *nevirapine BPCRS* in solution A. Dilute with the dissolution medium to produce a solution containing 0.0056% w/v of *nevirapine BPCRS*.
(3) 0.5% w/v of *nevirapine BPCRS* and 0.75% w/v of *methyl parahydroxybenzoate* in solution A. Dilute with the dissolution medium to produce a solution containing 0.004% w/v of *nevirapine BPCRS* and 0.006% w/v of *methyl parahydroxybenzoate*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 3.9 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Symmetry 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 10 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 5 minutes.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to nevirapine and methyl parahydroxybenzoate is at least 5.0.

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 80% (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 oral suspension containing the equivalent of 60 mg of nevirapine in 40 mL of *methanol*, and dilute to 200 mL with *water*.
(2) Dilute 1 volume of solution (1) to 100 volumes with *water*. Dilute 1 volume of this solution to 5 volumes with *water*.
(3) Dissolve the contents of a vial of *nevirapine for peak identification EPCRS* in 2 mL of *methanol (80%)*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *cyanosilyl silica gel for chromatography* (3.5 µm) (Zorbax SB-CN is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 35°.
(e) Use a detection wavelength of 254 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Solution B: Dissolve 6.8 g of *potassium dihydrogen orthophosphate* in 950 mL of *water*, and adjust to pH 3.0 with *orthophosphoric acid*. Dilute to 1000 mL with *water* and filter through a 0.45-µm membrane filter.

Mobile phase A: 3 volumes of *acetonitrile* and 97 volumes of solution B.

Mobile phase B: 24 volumes of *acetonitrile* and 76 volumes of solution B.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-3	100	0	isocratic
3-33	100→0	0→100	linear gradient
33-34	0→100	100→0	linear gradient
34-42	100	0	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to nevirapine (retention time about 23 minutes) are: impurity B, about 0.9; impurity A, about 1.1; impurity C, about 1.2

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 1.7.

the *resolution* between the peaks due to nevirapine and impurity A 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 the area of the principal peak in the chromatogram obtained with solution (2) (0.2%).

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

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

(1) Mix with the aid of ultrasound a weighed quantity of the oral suspension containing the equivalent of 60 mg of nevirapine in 40 mL of *methanol*, and dilute to 200 mL with *water*.
(2) 0.25% w/v of *nevirapine BPCRS* in *methanol*. Dilute 3 volumes to 25 volumes with *water*.
(3) Dissolve the contents of a vial of *nevirapine for peak identification EPCRS* in 2 mL of *methanol (80%)*.

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 B and nevirapine is at least 1.7.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the oral suspension, Appendix V G, and calculate the content of nevirapine, $C_{15}H_{14}N_4O$, weight in volume, using the declared content of $C_{15}H_{14}N_4O$ in *nevirapine BPCRS*.

IMPURITIES

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