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

Venlafaxine Tablets

General Notices

Action and use

Inhibition of 5HT and noradrenaline reuptake; antidepressant.

DEFINITION

Venlafaxine Tablets contain Venlafaxine Hydrochloride.

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

Content of venlafaxine, $C_{17}H_{27}NO_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the powdered tablets containing the equivalent of 0.35 g of venlafaxine with 100 mL of a mixture of 30 volumes of *cyclohexane* and 70 volumes of *dichloromethane* for 30 minutes, filter and evaporate the filtrate to dryness. Wash the residue with a mixture of 30 volumes of *cyclohexane* and 70 volumes of *dichloromethane*, filter and dry the residue. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of venlafaxine hydrochloride *(RS 439)*.

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 *water*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 45 minutes withdraw a sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with the dissolution medium if necessary, to give a solution expected to contain the equivalent of about 0.0025% w/v of venlafaxine, at the maximum at 274 nm, Appendix II B using *water* in the reference cell.
(2) Measure the *absorbance* of a 0.0025% w/v solution of *venlafaxine hydrochloride BPCRS* using *water* in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of venlafaxine, $C_{17}H_{27}NO_2$, in the medium from the absorbances obtained and using the declared content of $C_{17}H_{27}NO_2$,HCl in *venlafaxine hydrochloride BPCRS*. Each mg of $C_{17}H_{27}NO_2$,HCl is equivalent to 0.884 mg of $C_{17}H_{27}NO_2$.

LIMITS

The amount of venlafaxine 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 in the mobile phase A.

(1) Mix with the aid of ultrasound a quantity of the powdered tablets containing the equivalent of 200 mg of venlafaxine with 80 mL of a 2.4% v/v solution of *orthophosphoric acid*, shake for a further 30 minutes, cool, add sufficient *water* to produce 100 mL, mix and centrifuge; use the supernatant liquid.
(2) Dilute 1 volume of solution (1) to 500 volumes.
(3) 0.2% w/v of *venlafaxine impurity standard BPCRS*.
(4) Dilute 25 volumes of solution (2) to 100 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Partisil ODS 3 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 226 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A 1 volume of *triethylamine*, 20 volumes of *acetonitrile* and 80 volumes of *water* adjusted to pH 3.5 with *orthophosphoric acid*.

Mobile phase B 1 volume of *triethylamine*, 50 volumes of *acetonitrile* and 50 volumes of *water* adjusted to pH 3.5 with *orthophosphoric acid*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-20	100	0	isocratic
20-30	100→0	0→100	linear gradient
30-45	0	100	isocratic
45-48	0→100	100→0	re-equilibration
48-60	100	0	isocratic

Under the prescribed conditions, the retention time of venlafaxine is about 13 minutes.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution factor* between the peaks due to impurity D and venlafaxine is at least 1.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity D or impurity F is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2% of each);

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 all the *secondary peaks* is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with an area less than that of the principal peak in the chromatogram obtained with solution (4) (0.05%).

ASSAY

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

(1) Mix a quantity of the powdered tablets containing the equivalent of 50 mg of venlafaxine with 200 mL of a 0.2% v/v solution of *orthophosphoric acid* for 15 minutes with the aid of ultrasound and shake vigorously. Mix for a further 15 minutes with the aid of ultrasound, cool, add sufficient of a 0.2% v/v solution of *orthophosphoric acid* to produce 250 mL, mix and centrifuge. To 2 volumes of the supernatant liquid add sufficient of the mobile phase to produce 5 volumes.
(2) 0.009% w/v of *venlafaxine hydrochloride BPCRS*.
(3) 0.01% w/v of *venlafaxine impurity standard BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *octylsilyl silica gel for chromatography* (5 µm) (Zorbax C8 is suitable)
(b) Use isocratic 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 226 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

25 volumes of *acetonitrile* and 75 volumes of a 1% v/v solution of *triethylamine*, previously adjusted to pH 3.0 with *orthophosphoric acid*.

Under the prescribed conditions, the retention time of venlafaxine is about 5 minutes, if necessary adjust the *acetonitrile* content of the mobile phase.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution factor* between the peaks due to impurity D and venlafaxine is at least 1.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{17}H_{27}NO_2$ in the tablets using the declared content of $C_{17}H_{27}NO_2$,HCl in *venlafaxine hydrochloride BPCRS*. Each mg of $C_{17}H_{27}NO_2$,HCl is equivalent to 0.884 mg of $C_{17}H_{27}NO_2$.

LABELLING

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

IMPURITIES

The impurities limited by the requirements of this monograph include:

D. 1-[(1*RS*)-1-(4-methoxyphenyl)-2-(methylamino)ethyl]cyclohexanol (European Pharmacopoeia impurity D);
F. (2*RS*)-2-(cyclohex-1-enyl)-2-(4-methoxyphenyl)-*N,N*-dimethylethanamine (European Pharmacopoeia impurity F).