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

Escitalopram Oral Solution

General Notices

Action and use

Selective serotonin reuptake inhibitor; antidepressant.

DEFINITION

Escitalopram Oral Solution contains Escitalopram Oxalate in a suitable vehicle.

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

Content of escitalopram, $C_{20}H_{21}FN_2O$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Evaporate a quantity of the oral solution containing the equivalent of 100 mg of escitalopram to reduced volume under a stream of *nitrogen* and dried in a vacuum desiccator. Dissolve the residue in 20 mL of water and filter. Add 5 mL of 5M sodium hydroxide to the filtrate and extract with three 25-mL quantities of dichloromethane. Dry the combined organic layers over sodium sulfate and evaporate to dryness using a rotary evaporator at a temperature not exceeding 40°. The infrared absorption spectrum of the residue, Appendix II A, is concordant with the spectrum of *escitalopram BPCRS* treated in the same manner.
B. Complies with the test for Impurity K.

TESTS

Escitalopram impurity K (enantiomeric impurity)

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

(1) Shake a quantity of the oral solution containing the equivalent of 25 mg of escitalopram with 150 mL of the mobile phase, add sufficient of the mobile phase to produce 200 mL and filter.
(2) 0.0125% w/v of *citalopram hydrobromide BPCRS* (containing equal amounts of impurity K and escitalopram) in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6) mm packed with *protein derivative of silica gel for chiral separation R* (5 µm) (Ultron ES-OVM is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 0.6 mL per minute.
(d) Use a column temperature of 30°.
(e) Use a detection wavelength of 240 nm.
(f) Inject 15 µL of each solution.

(g) Allow the chromatography to run for twice the retention time of escitalopram.

MOBILE PHASE

15 volumes of *acetonitrile* and 85 volumes of *0.05M phosphate buffer solution pH 7.0*.

When the chromatograms are recorded under the prescribed conditions, the relative retention with respect to escitalopram (retention time, about 11 min) of impurity K is about 1.2.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2):

the *resolution* between the peaks due to escitalopram and impurity K is at least 1.3;

the *symmetry factors* for the peaks due to escitalopram and impurity K are between 0.8 and 4.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak due to impurity K is not greater than 2.0% by *normalisation*;

disregard any peak with an area less than 0.1% of that of the area of the peak due to impurity K.

Related substances

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

(1) To a quantity of the oral solution containing the equivalent of 50 mg of escitalopram add sufficient mobile phase A to produce 100 mL and filter.
(2) Dilute 1 volume of solution (1) to 100 volumes with mobile phase A and further dilute 2 volumes of this solution to 10 volumes with the same solvent.
(3) 0.05% w/v of *escitalopram for system suitability CRS* (containing impurity D) in mobile phase A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6) mm packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Luna C18 is suitable).
(b) Use gradient elution with the flow rate and mobile phase described below.
(c) Use a column temperature of 45°.
(d) Use detection wavelengths of 237 nm and 254 nm.
(e) Inject 20 µL of each solution.

MOBILE PHASE

Solution A 0.34% w/v of *potassium dihydrogen orthophosphate* adjusted to pH 3.0 with *orthophosphoric acid*.

Mobile phase A 10 volumes of *acetonitrile* and 90 volumes of solution A.

Mobile phase B 65 volumes of *acetonitrile* and 35 volumes of solution A.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Flow rate (mL/min)	Comment
0-2	95	5	1	isocratic
2-37	95→65	5→35	1	linear gradient
37-47	65→0	35→100	1	linear gradient
47-62	0	100	2	isocratic
62-64	0→95	100→5	1	linear gradient
64-67	95	5	1	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to escitalopram (retention time about 38 minutes) are: impurity F, about 0.1; impurity J, about 0.2; impurity G, about 0.5; impurity A, about 0.6; impurity B/M, about 0.8; impurity C/I/L, about 0.9; impurity D, about 0.95; impurity H, about 1.1.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3) at 237 nm, the *peak-to-valley ratio* is at least 5.0, where *Hp* is the height above the baseline of the peak due to impurity D and *Hv* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to escitalopram.

LIMITS

Calculate the amount of each impurity at both 237 nm and 254 nm using the area of the peak due to escitalopram from solution (2) at 237 nm.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity C, I and L is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

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 (at 237 mn) of any *secondary peaks* is not greater than 5 times the area of the principal peak in the chromatogram obtained with solution (2) (1%).

Disregard any peak with an area less than half the area of the principal peak in the chromatogram obtained with solution (2) at 237 nm (0.1%).

ASSAY

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

(1) To a quantity of the oral solution containing the equivalent of 50 mg of escitalopram add sufficient mobile phase to produce 100 mL and filter. Dilute 1 volume of the filtrate to 10 volumes with the mobile phase.
(2) 0.006% w/v of *citalopram hydrobromide BPCRS* in the mobile phase.
(3) 0.05% w/v of *escitalopram for system suitability EPCRS* (containing impurity D) in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Luna C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 45°.
(e) Use a detection wavelength of 237 nm.
(f) Inject 20 µL of each solution.
(g) Allow the chromatography to proceed for 1.5 times the retention time of escitalopram (about 11 minutes).

MOBILE PHASE

30 volumes of *acetonitrile* and 70 volumes of Solution A.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *peak-to-valley ratio* is at least 5.0, where *Hp* is the height above the baseline of the peak due to impurity D and *Hv* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to escitalopram.

DETERMINATION OF CONTENT

Calculate the content of $C_{20}H_{21}FN_2O$, in the oral solution from the chromatograms obtained and using the declared content of $C_{20}H_{21}FN_2O$, in *escitalopram oxalate BPCRS*.

STORAGE

Escitalopram Oral Solution should be stored below 25°.

LABELLING

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

IMPURITIES

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