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

Paroxetine Tablets

General Notices

Action and use

Selective serotonin reuptake inhibitor; antidepressant.

DEFINITION

Paroxetine Tablets contain Paroxetine Hydrochloride Hemihydrate or Paroxetine Hydrochloride. They are coated.

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

PRODUCTION

The manufacturing process of Paroxetine Hydrochloride, used in the formulation of Paroxetine Tablets, is validated to show that the content of 4-(4′-fluorophenyl)-1-methyl-1,2,3,6-tetrahydropyridine is not more than 1 ppm.

Content of anhydrous paroxetine hydrochloride, $C_{19}H_{20}FNO_3,HCl$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. The *light absorption*, Appendix II B, in the range 230 to 350 nm of the final solution obtained in the Dissolution test exhibits a maximum at 294 nm.
B. In the Assay, the principal peak in the chromatogram obtained with solution (1) has the same retention time as the principal peak in the chromatogram obtained with solution (2).

TESTS

Dissolution

Comply with the requirements for Monographs of the British Pharmacopoeia in 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

(1) After 45 minutes withdraw a sample of the medium and filter through a plastic filter with a GF/A filter (Millipore Swinnex is suitable). Measure the a*bsorbance* of the filtrate, suitably diluted with the dissolution medium if necessary, at the maximum at 294 nm, Appendix II B, using the dissolution medium in the reference cell.
(2) Measure the *absorbance* of a suitable solution of *paroxetine hydrochloride hemihydrate BPCRS* in 0.1M *hydrochloric acid* at the maximum at 294 nm using the dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of paroxetine hydrochloride, $C_{19}H_{20}FNO_3$,HCl, in the medium from the absorbances obtained and from the declared content of $C_{19}H_{20}FNO_3$,HCl in *paroxetine hydrochloride hemihydrate BPCRS*.

Related substances

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

(1) Shake a quantity of the powdered tablets containing the equivalent of 50 mg of anhydrous paroxetine hydrochloride with 10 mL of *methanol* for 30 minutes. Filter through a 0.45-µm membrane filter (Gelman acrodisc GHP is suitable), dilute 1 volume of the solution with 1 volume of mobile phase B.
(2) Dilute 1 volume of solution (1) to 50 volumes with mobile phase A and further dilute 1 volume of the resulting solution to 10 volumes with mobile phase A.
(3) 0.25% w/v of *paroxetine impurity standard BPCRS* in mobile phase A.
(4) 0.00075% w/v of *paroxetine impurity A EPCRS* in mobile phase A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *cyanosilyl silica gel for chromatography* (5 µm) (Spherisorb CN is suitable).
(b) Use gradient 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 265 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A Equal volumes of *acetonitrile* and phosphate buffer pH 6.0 prepared by dissolving 4.9 g of *orthophosphoric acid* in about 800 mL of *water*, adjusting the pH to 6.0 with 1M *sodium hydroxide* and diluting to 1000 mL with *water*.

Mobile phase B Phosphate buffer pH 6.0 prepared by dissolving 4.9 g of *orthophosphoric acid* in about 800 mL, adjusting the pH to 6.0 with 1M *sodium hydroxide* and diluting to 1000 mL with *water*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-20	25→75	75→25	linear gradient
20-30	75	25	isocratic
30-35	75→25	25→75	linear gradient
35-45	25	75	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) closely resembles the reference chromatogram supplied with *paroxetine impurity standard BPCRS*.

LIMITS

Identify any peak due to impurity I in the chromatogram obtained with solution (1), using the chromatogram obtained with solution (3), and multiply the area of this peak by a correction factor of 2.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity A is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%);

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

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 any other *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 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.

(1) Disperse with the aid of ultrasound a quantity of powdered tablets containing the equivalent of 25 mg of anhydrous paroxetine hydrochloride in 70 mL of *water* and 5 mL of 0.05M *hydrochloric acid*. Mix with the aid of ultrasound until all the granular material has dispersed. Add 150 mL of *propan-2-ol*, shake thoroughly and mix with the aid of ultrasound with occasional swirling for 15 minutes. Cool, add sufficient *propan-2-ol* to produce 250 mL, filter through a glass microfibre filter (Whatman GF/F is suitable) and use the filtrate.
(2) 0.01% w/v of *paroxetine hydrochloride hemihydrate BPCRS* in a solution containing 1 volume of 0.01M *hydrochloric acid*, 14 volumes of *water* and 35 volumes of *propan-2-ol*.
(3) 0.25% w/v of *paroxetine impurity standard BPCRS* in mobile phase A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *cyanosilyl silica gel for chromatography* (5 µm) (Spherisorb CN is suitable).
(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 265 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Equal volumes of *acetonitrile* and phosphate buffer pH 6.0 prepared by dissolving 4.9 g of *orthophosphoric acid* in about 800 mL of *water*, adjusting the pH to 6.0 with 1M *sodium hydroxide* and diluting to 1000 mL with *water*.

SYSTEM SUITABILITY

The test is not valid unless, the chromatogram obtained with solution (3) closely resembles the chromatogram supplied with *paroxetine impurity standard BPCRS*.

DETERMINATION OF CONTENT

Calculate the content of paroxetine hydrochloride, $C_{19}H_{20}FNO_3$,HCl, in the tablets using the declared content of $C_{19}H_{20}FNO_3$,HCl in *paroxetine hydrochloride hemihydrate BPCRS*.

LABELLING

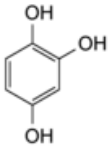
When the active ingredient is Paroxetine Hydrochloride Hemihydrate, the quantity is stated in terms of the equivalent amount of anhydrous paroxetine hydrochloride.

STORAGE

Paroxetine Tablets should be protected from light.

IMPURITIES

The impurities limited by the requirements of this monograph include impurity A listed under Paroxetine Hydrochloride and Paroxetine Hydrochloride Hemihydrate, impurities B and I listed under Paroxetine Hydrochloride and the following:



1. 1,2,4-trihydroxybenzene.