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

Zopiclone Tablets

General Notices

Action and use

Non-benzodiazepine hypnotic.

DEFINITION

Zopiclone Tablets contain Zopiclone.

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

Content of zopiclone, $C_{17}H_{17}ClN_6O_3$

95.0 to 105.0% of the stated amount.

Carry out all of the following procedures protected from light.

IDENTIFICATION

Shake a quantity of the powdered tablets containing 37.5 mg of Zopiclone with 30 mL of *acetone*, add sufficient *acetone* to produce 50 mL and filter. Evaporate the filtrate to dryness on a water bath and dry the residue in an oven at 60° for 2 hours. The *infrared absorption spectrum* of the dried residue, Appendix II A, is concordant with the *reference spectrum* of zopiclone *(RS 430)*.

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 500 mL of *0.1M hydrochloric acid*, at a temperature of 37°, as the dissolution 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, at the maximum at 305 nm, Appendix II B using *0.1M hydrochloric acid* in the reference cell.
(2) Measure the *absorbance* of a suitable solution of zopiclone *BPCRS* using *0.1M hydrochloric acid* in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of zopiclone, $C_{17}H_{17}ClN_6O_3$, in the medium using the declared content of $C_{17}H_{17}ClN_6O_3$ in *zopiclone BPCRS*.

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 37.5 mg of Zopiclone with 50 mL of the mobile phase for 30 minutes, shake for a further 20 minutes. Cool the solution and add sufficient of the mobile phase to produce 100 mL, mix and filter through a 0.45-µm PTFE filter.
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase.
(3) 0.0006% w/v of *2-amino-5-chloropyridine BPCRS* and 0.0001% w/v of each *zopiclone BPCRS* *and* *zopiclone oxide EPCRS* in the mobile phase.
(4) Dilute 1 volume of solution (2) to 10 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *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 1.5 mL per minute.
(d) Use a detection wavelength of 303 nm.
(e) Use a column temperature of 30°.
(f) Inject 20 µL of each solution.
(g) Allow the chromatography to proceed for twice the retention time of zopiclone.

When the chromatograms are recorded under the prescribed conditions the retention times relative to zopiclone (retention time, about 26 minutes) are: 2-amino-5-chloropyridine, about 0.3 and zopiclone oxide, about 0.8.

MOBILE PHASE

375 volumes of *acetonitrile* and 625 volumes of a solution containing 0.5% w/v of *sodium dodecyl sulfate* and 0.01% w/v of *sodium dihydrogen orthophosphate* previously adjusted to pH 4.0 with *orthophosphoric acid*.

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (3), the *resolution* between the peaks due to zopiclone and zopiclone-*N*-oxide is at least 3.0;

in the chromatogram obtained with solution (4), the *signal-to-noise ratio* of the principal peak is not less than 10.

LIMITS

In the chromatogram obtained with solution (1):

the area of the peak due to 2-amino-5-chloropyridine is not greater than the area of the peak due to 2-amino-5-chloropyridine in solution (3) (1.5%);

excluding 2-amino-5-chloropyridine, the area of any *secondary peak* is not greater than 0.3 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%);

the sum of the impurities is not greater than 2%.

Disregard any peak with an area less than the area of the principal peak in solution (4) (0.1%).

Uniformity of content

Tablets containing less than 2 mg and/or less than 2% w/w of Zopiclone comply with the requirements stated under Tablets using the following method of analysis.

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

(1) Finely crush one tablet, add sufficient of the mobile phase to produce a solution with an expected concentration of 0.0075% w/v, shake and filter.

(2) 0.0075% w/v of *zopiclone BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *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 1.5 mL per minute.
(d) Use a detection wavelength of 303 nm.
(e) Use a column temperature of 30°.
(f) Inject 10 µL of each solution.

MOBILE PHASE

1 volume of *acetonitrile* and 1 volume of a solution containing 0.5% w/v of *sodium dodecyl sulfate* and 0.1% w/v of *sodium dihydrogen orthophosphate*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the *symmetry factor* of the peak due to zopiclone is at most 1.4.

DETERMINATION OF CONTENT

Calculate the content of $C_{17}H_{17}ClN_6O_3$ in the tablets using the declared content of $C_{17}H_{17}ClN_6O_3$ in *zopiclone BPCRS*.

ASSAY

For tablets containing less than 2 mg and/or less than 2% w/w of zopiclone

Use the average of the individual results determined in the test for Uniformity of content.

For tablets containing 2 mg or more and 2% w/w or more of zopiclone

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

(1) Shake a quantity of the powdered tablets containing 37.5 mg of Zopiclone with 60 mL of the mobile phase for 20 minutes, add sufficient of the mobile phase to produce 500 mL, mix and filter (Whatman GF/C is suitable), discarding the first 10 mL of filtrate.
(2) 0.0075% w/v of *zopiclone BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Uniformity of content may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the *symmetry factor* of the peak due to zopiclone is at most 1.4.

DETERMINATION OF CONTENT

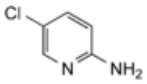
Calculate the content of $C_{17}H_{17}ClN_6O_3$ in the tablets using the declared content of $C_{17}H_{17}ClN_6O_3$ in *zopiclone BPCRS*.

STORAGE

Zopiclone Tablets should be protected from light.

IMPURITIES

In addition to the impurities listed under Zopiclone, the impurities limited by the requirements of this monograph include:



2-amino-5-chloropyridine.