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

Rizatriptan Tablets

General Notices

Action and use

Serotonin $5HT_1$ receptor agonist; treatment of migraine.

DEFINITION

Rizatriptan Tablets contain Rizatriptan Benzoate.

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

Content of rizatriptan, $C_{15}H_{19}N_5$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Add 10 mL of *methanol* to a quantity of powdered tablets containing the equivalent of 50 mg of rizatriptan, mix with the aid of ultrasound for 5 minutes, filter through a 0.4-µm PTFE filter, evaporate the filtrate and dry under reduced pressure for 1 hour. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the reference spectrum of rizatriptan benzoate (*RS 474*).

TESTS

Dissolution

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

TEST CONDITIONS

(a) Use Apparatus 2 and rotate the paddle at 50 revolutions per minute.
(b) Use 900 mL of *water*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 15 minutes withdraw a 15-mL sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with *water*, if necessary, to produce a solution expected to contain the equivalent of about 0.0004% w/v of rizatriptan at the maximum at 226 nm, Appendix II B, using *water* in the reference cell.
(2) Measure the *absorbance* of a solution of 0.00058% w/v of *rizatriptan benzoate BPCRS* using *water* in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of rizatriptan $C_{15}H_{19}N_5$ in the medium from the absorbances obtained and using the declared content of $C_{15}H_{19}N_5$ in *rizatriptan benzoate BPCRS*.

LIMITS

The amount of rizatriptan released is not less than 80% (Q) of the stated amount.

Related substances

Prepare a solution containing 1 volume of *acetonitrile R1* and 4 volumes of 0.05M *ammonium acetate* (solution A).

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

(1) To a quantity of the powdered tablets containing the equivalent of 40 mg of rizatriptan add 60 mL of solution A, mix with the aid of ultrasound, dilute to 100 mL with solution A and filter through a 0.4-µm PTFE filter. Dilute 1 volume of the filtrate to 10 volumes.
(2) Dilute 1 volume of solution (1) to 100 volumes with solution A and dilute 1 volume of the resulting solution to 5 volumes with solution A.
(3) To 5 mL of a solution containing 0.0058% w/v of *rizatriptan benzoate BPCRS* in solution A add 0.2 mL of *hydrogen peroxide solution (100 vol)*. Mix, heat in an oven at 60° for 30 minutes and allow to stand for 24 hours before use (preparation of impurity H).
(4) 0.005% w/v of *benzoic acid* in solution A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Waters Symmetry C18 is suitable), fitted with a stainless steel guard column (2 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Waters Sentry C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 45°.
(e) Use a detection wavelength of 226 nm.
(f) Inject 10 µL of each solution.
(g) For solution (1) allow the chromatography to proceed for twice the retention time of rizatriptan.

MOBILE PHASE

15 volumes of *acetonitrile R1* and 85 volumes of a phosphate buffer solution prepared as follows: dissolve 1.7 g of *potassium dihydrogen orthophosphate* and 0.94 g of *sodium hexanesulfonate* in 900 mL of *water*, adjust the pH to 6.8 with 19M *sodium hydroxide* and dilute to 1000 mL with *water*.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to rizatriptan (retention time about 10 minutes) are: benzoic acid, about 0.3 and impurity H, about 0.5.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between benzoic acid and impurity H 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 any *secondary peaks* is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (0.4%).

Disregard any peak due to benzoic acid and with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

Prepare a solution containing 1 volume of *acetonitrile R1* and 4 volumes of 0.05M *ammonium acetate* (Solution A).

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

(1) To a quantity of the powdered tablets containing the equivalent of 40 mg of rizatriptan add 60 mL of solvent A, mix with the aid of ultrasound, dilute to 100 mL with solution A and filter through a 0.4-µm PTFE filter. Dilute 1 volume of the filtrate to 10 volumes.
(2) 0.0058% w/v of *rizatriptan benzoate BPCRS* in solution A.
(3) Prepare impurity H as follows. Add 0.2 mL of *hydrogen peroxide solution (100 vol)* to 5 mL of solution (2). Mix, heat in an oven at 60° for 30 minutes and allow to stand for 24 hours before use.

CHROMATOGRAPHIC CONDITIONS

The chromatographic procedure described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless in solution (3) the *resolution* between the peaks due to benzoic acid and impurity H is at least 3.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{15}H_{19}N_5$ in the tablets using the declared content of $C_{15}H_{19}N_5$ in *rizatriptan benzoate BPCRS*.

LABELLING

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

IMPURITIES

The impurities limited by the requirements of this monograph include impurity H listed under Rizatriptan Benzoate.