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Rizatriptan Orodispersible Tablets

General Notices

Orodispersible Rizatriptan Tablets

Details for the public consultation of this monograph are as follows:

EAG/Panel/Working Party	**Medicinal Chemicals 1**
Contact Details	graziella.li-ship@mhra.gov.uk jonathan.campbell@mhra.gov.uk
Deadline for Comment	30th June 2026
Target Publication Date (subject to change)	BP 2028
Notes	Revised monograph **Dissolution** Sample dissolution time revised

Action and use

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

DEFINITION

Rizatriptan Orodispersible Tablets contain Rizatriptan Benzoate in a suitable orodispersible basis.

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

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

93.4 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions in *methanol (30%)*.
(1) To a quantity of the powdered tablets containing the equivalent of 68.8 mg of rizatriptan add 7 mL, shake well, filter and dilute to 10 mL.
(2) 1.0% w/v *rizatriptan benzoate BPCRS*.
(3) 1.0% w/v *benzoic acid*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel F_{254}*.

(b) Use the mobile phase as described below.
(c) Apply 5 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air and examine under *ultraviolet light (254 nm)*.
(f) Expose the plate to iodine vapour until maximum contrast between the spots is obtained and examine in daylight.

MOBILE PHASE

1 volume of 18M *ammonia*, 20 volumes of *methanol* and 80 volumes of *dichloromethane*.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) when examined under ultraviolet light corresponds in position to that in the chromatogram obtained with solution (3) (benzoic acid).

The principal spot in the chromatogram obtained with solution (1) when exposed to iodine vapour corresponds in position to that in the chromatogram obtained with solution (2) (rizatriptan).

B. In the Assay, the principal peaks in the chromatogram obtained with solution (1) have the same retention time as those in the chromatogram obtained with solution (2).

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 0.00055% w/v of rizatriptan, at the maximum at 278 nm, Appendix II B, using *water* in the reference cell.
(2) Measure the *absorbance* of a solution of 0.0008% 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 9 volumes of 0.025M *potassium dihydrogen orthophosphate* (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 50 mg of rizatriptan add 60 mL of solvent A, mix with the aid of ultrasound, dilute to 100 mL 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) Prepare impurity H as follows. To 5 mL of a solution containing 0.0075% 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.
(4) Prepare impurity 1, if aspartame is present, as follows. To a 50-mL round-bottomed flask add 24 mg of *rizatriptan benzoate BPCRS*, 2 mL of *methanol* and 2 mL of *dimethyl carbonate* and mix well. Heat under a reflux condenser for 2 hours at 125°, cool and dilute 1 volume to 100 volumes with solution A. To 1 mL of the resulting solution add 20 µL of 10M *sodium hydroxide*, incubate at room temperature for 2 hours and neutralise to pH 7 with approximately 30 µL of *6M hydrochloric acid*.
(5) 0.01% w/v of *benzoic acid* in solution A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm x 4.6 mm) packed with *base-deactivated end-capped octylsilyl silica gel for chromatography* (5 µm) (YMC Basic is suitable).
(b) Use isocratic elution using the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 30°.
(e) Use a detection wavelength of 226 nm.
(f) Inject 20 µL of each solution.
(g) For solution (1) allow the chromatography to proceed for twice the retention time of rizatriptan.

MOBILE PHASE

16 volumes of *acetonitrile R1* and 84 volumes of a phosphate buffer solution prepared by weighing 3.4 g of *potassium dihydrogen orthophosphate* and 2.0 g of *sodium hexanesulfonate* into a 1000 mL flask, dissolve in 900 mL of *water*, adjust the pH to 7.5 with 19M *sodium hydroxide* and dilute to volume with *water*.

SYSTEM SUITABILITY

The relative retention times with reference to rizatriptan (retention time about 16 minutes) are: benzoic acid, about 0.2; impurity H, about 0.3; impurity I, about 0.8 and impurity 1, about 0.9.

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 peak corresponding to rizatriptan impurity H 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 peak corresponding to rizatriptan impurity I is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (0.4%);

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 *secondary peaks* is not greater than 10 times the area of the principal peak obtained with solution (2) (2%).

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

For formulations containing aspartame

SYSTEM SUITABILITY

The test is not valid unless in the chromatogram obtained with solution (4) the *resolution* between impurity 1 and rizatripan is at least 3.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to rizatriptan impurity 1 is not greater than 5.5 times the area of the principal peak in the chromatogram obtained with solution (2) (1.1%).

ASSAY

Prepare a solution containing 1 volume of *acetonitrile R1* and 9 volumes of 0.025M *potassium dihydrogen orthophosphate* (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 50 mg of rizatriptan add 60 mL of solvent A, mix with the aid of ultrasound, dilute to 100 mL and filter through a 0.4-µm PTFE filter. Dilute 1 volume of the filtrate to 10 volumes with solution A.
(2) 0.0075% 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 (1). Mix, heat in an oven at 60° for 30 minutes and allow to stand for 24 hours before use.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

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.

DETERMINATION OF CONTENT

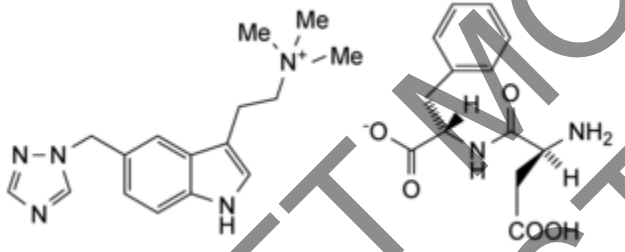
Calculate the content of $C_{15}H_{19}N_5$ in the tablets using the declared content of $C_{15}H_{19}N_5$ in *rizatriptan benzoate BPCRS*.

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 impurities A, H and I listed under Rizatriptan Benzoate and the following:



1. *N,N,N*-trimethyl-2-{[(1*H*-1,2,4-triazol-1-yl)methyl]-1*H*-indol-3-yl}ethanaminium L-aspartyl-L-phenylalaninate.