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Rizatriptan Benzoate Orally Disintegrating Tablets

DEFINITION

Rizatriptan Benzoate Orally Disintegrating Tablets contain an amount of rizatriptan benzoate ($C_{15}H_{19}N_5 \cdot C_7H_6O_2$) equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of rizatriptan ($C_{15}H_{19}N_5$).

IDENTIFICATION

- **A.** The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.
- **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Buffer: Transfer 3.4 g of monobasic potassium phosphate and 2.0 g of 1-heptanesulfonic acid, sodium salt to a 1-L volumetric flask. Add 900 mL of *water*. Adjust with 50% (w/w) sodium hydroxide to a pH of 7.5, and dilute with water to volume.

Mobile phase: Acetonitrile and *Buffer* (16:84)

Diluent: Acetonitrile and 0.025 M monobasic potassium phosphate (10:90)

Standard solution: 0.07 mg/mL of USP Rizatriptan Benzoate RS in *Diluent*

Sample stock solution: Nominally 0.5 mg/mL of rizatriptan in *Diluent* prepared as follows. Transfer NLT 10 Tablets to a suitable volumetric flask. Add 25%–50% of the flask volume of *Diluent*, and swirl until the Tablets have disintegrated completely. Dilute with *Diluent* to volume.

Sample solution: Nominally 0.05 mg/mL of rizatriptan free base from the *Sample stock solution* in *Diluent*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 226 nm. For *Identification B*, use a diode array detector in the range of 210–400 nm.

Column: 4.6-mm × 25-cm; 5-µm packing L7

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 1.5 times the retention time of rizatriptan

System suitability

Sample: *Standard solution*

[Note—See *Table 1* for relative retention times.]

Suitability requirements

Tailing factor: NMT 3.5

Relative standard deviation: NMT 2.0% for the rizatriptan peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of rizatriptan ($C_{15}H_{19}N_5$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Rizatriptan Benzoate RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of rizatriptan in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of rizatriptan free base, 269.35

M_{r2} = molecular weight of rizatriptan benzoate, 391.47

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Test 1

Medium: *water*; 900 mL

Apparatus 2: 50 rpm

Time: 5 min

Standard solution: (*L*/625) mg/mL of USP Rizatriptan Benzoate RS in *Medium*, where *L* is the label claim of rizatriptan in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable membrane filter of 10-µm pore size.

Instrumental conditions

Mode: UV

Analytical wavelengths: 278 and 320 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of rizatriptan ($C_{15}H_{19}N_5$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

A_U = absorbance of rizatriptan from the *Sample solution*, corrected for the absorbance at 320 nm

A_S = absorbance of rizatriptan from the *Standard solution*, corrected for the absorbance at 320 nm

C_S = concentration of USP Rizatriptan Benzoate RS in the *Standard solution* (mg/mL)

V = volume of *Medium*, 900 mL

M_{r1} = molecular weight of rizatriptan free base, 269.35

M_{r2} = molecular weight of rizatriptan benzoate, 391.47

L = label claim of rizatriptan (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of rizatriptan ($C_{15}H_{19}N_5$) is dissolved.

Test 2: If the product complies with this procedure, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: Water, deaerated; 900 mL

Apparatus 2: 50 rpm

Time: 10 min

Buffer: Dissolve 2.7 g of monobasic potassium phosphate in 1 L of water. Add 2 mL of triethylamine and adjust with diluted phosphoric acid (1 in 10) to a pH of 5.0.

Mobile phase: Methanol and *Buffer* (10:90)

Standard solution: (*L*/625) mg/mL of USP Rizatriptan Benzoate RS in *Medium*, where *L* is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable membrane filter of 0.45-µm pore size.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 225 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of rizatriptan

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of rizatriptan ($C_{15}H_{19}N_5$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2}) \times V \times (1/L) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Rizatriptan Benzoate RS in the *Standard solution* (mg/mL)

M_{r1} = molecular weight of rizatriptan, 269.35

M_{r2} = molecular weight of rizatriptan benzoate, 391.47

V = volume of *Medium* (900 mL)

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of rizatriptan ($C_{15}H_{19}N_5$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

Mobile phase, Diluent, Standard solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability stock solution A: Solution containing rizatriptan *N*-oxide prepared as follows. Rinse a suitable flask with hydrogen peroxide. Heat the flask in an oven for about 10 min. Allow the flask to cool and rinse with water. Transfer 5 mL of *Standard solution* to the flask, add 0.2 mL of hydrogen peroxide, and tightly stopper. Mix well and heat in an oven at 60° for about 30 min. Allow to stand for 24 h. [Note—This solution is stable for at least 7 days at room temperature.]

System suitability stock solution B: Solution containing an *N*-methyl adduct of rizatriptan prepared as follows. Dissolve 10 mg of USP Rizatriptan Benzoate RS in 1 mL of methanol in a suitable round-bottom flask. Add 1 mL of dimethylcarbonate and mix by swirling. Reflux the resulting solution over a heating mantle at 125° for NLT 2 h. Allow the solution to cool, and dilute 1 mL of the resulting solution with *Diluent* to 100 mL. [Note—This solution is stable for 3 months under refrigerated conditions.] Transfer 10 mL of the resulting solution to a suitable container with a stopper. Add 0.2 mL of 6 M sodium hydroxide solution, and allow the solution to remain at room temperature for NLT 2 h. Neutralize the solution with 0.3 mL of 6 M hydrochloric acid.

System suitability solution: *System suitability stock solution A, System suitability stock solution B,* and *Standard solution* (4:4:2)

Sensitivity solution: 0.07 µg/mL of USP Rizatriptan Benzoate RS from the *Standard solution* in *Diluent*

System suitability

Samples: *Standard solution*, *System suitability solution*, and *Sensitivity solution*

Suitability requirements

Resolution: NLT 2 between *N*-methyl adduct and rizatriptan, *System suitability solution*

Tailing factor: NMT 3.5, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Sample: *Sample solution*

Calculate the percentage of each degradation product in the portion of Tablets taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = response of each individual degradation product from the *Sample solution*

r_T = sum of all the areas of rizatriptan and all the degradation products excluding the benzoic acid peak and process impurities from the *Sample solution*

Acceptance criteria: See *Table 1*. Reporting threshold for the impurities is 0.1%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Benzoic acid[a]	0.2	—
Rizatriptan *N*-oxide[b]	0.3	0.5
Aspartame[c]	0.4	—
Rizatriptan desmethyl[d]	0.8	0.4
Rizatriptan *N*-methyl adduct[e]	0.9	1.5
Rizatriptan	1.0	—
Any individual unspecified degradation product	—	0.2
Total degradation products[f]	—	2.0

[a] This is the counterion. It is not to be reported or included in the total degradation products for the drug product.

[b] 2-{5-[(1*H*-1,2,4-Triazol-1-yl)methyl]-1*H*-indol-3-yl}-*N*,*N*-dimethylethanamine oxide.

[c] Excipient; may not be present in all sample formulations.

[d] 2-{5-[(1*H*-1,2,4-Triazol-1-yl)methyl]-1*H*-indol-3-yl}-*N*-methylethanamine. [NOTE—May not be present in all formulations.]

[e] 2-{5-[(1*H*-1,2,4-Triazol-1-yl)methyl]-1*H*-indol-3-yl}-*N*,*N*,*N*-trimethylethan-1-aminium.

[f] Process impurities are controlled in the drug substance and are not to be reported or included in the total degradation products for the drug product.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed, light-resistant containers. Store at controlled room temperature.
- **LABELING:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP REFERENCE STANDARDS** ⟨11⟩
  USP Rizatriptan Benzoate RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
RIZATRIPTAN BENZOATE ORALLY DISINTEGRATING TABLETS	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

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