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# Rizatriptan Benzoate Tablets

## DEFINITION

Rizatriptan Benzoate 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

***Change to read:***

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197M**▲ (CN 1-May-2020)

**Sample:** Grind a suitable number of Tablets containing NLT 125 mg of rizatriptan. Transfer a suitable amount of powder equivalent to NLT 100 mg of rizatriptan to a suitable flask to obtain a 5 mg/mL solution. Add 75% of the flask volume of methanol. Shake vigorously to disperse the powder. Dilute with methanol to volume. Pass a portion through a suitable filter. Evaporate the filtrate under a stream of nitrogen. Prepare a mull of the residue with mineral oil.

**Acceptance criteria:** The spectrum of the *Sample* corresponds to that of a similarly prepared Standard.

• **B.** The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution,* as obtained in the *Assay.*

## ASSAY

• **Procedure**

**Buffer:** Dissolve 1.7 g of monobasic potassium phosphate and 0.9 g of sodium 1-hexanesulfonate to a 1-L volumetric flask. Add 900 mL of water. Adjust with 50% (w/w) sodium hydroxide solution to a pH of 6.8. Dilute with water to volume.

**Mobile phase:** Acetonitrile and *Buffer* (15:85)

**Diluent:** Acetonitrile and 0.05 M ammonium acetate (20:80)

**Standard solution:** 0.06 mg/mL of USP Rizatriptan Benzoate RS in *Diluent*

**Sample stock solution:** Nominally 0.2 mg/mL of rizatriptan in *Diluent* prepared as follows. Transfer NLT 10 Tablets to a suitable volumetric flask. Add 10%–20% of the flask volume of *Diluent*. Swirl until the Tablets have disintegrated completely. Dilute with *Diluent* to volume. Stir the solution for 90–150 min. Centrifuge a portion of the resulting solution. Use the supernatant to prepare the *Sample solution*.

**Sample solution:** Nominally 0.04 mg/mL of rizatriptan from the supernatant of the *Sample stock solution* and *Diluent*

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 226 nm

**Column:** 4.6-mm × 25-cm; 5-µm packing L1. [Note—A suitable guard column may be used if necessary.]

**Column temperature:** 45°

**Flow rate:** 1 mL/min

**Injection volume:** 10 µL

**Run time:** NLT 2.5 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 for the rizatriptan peak

**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 of rizatriptan from the *Sample solution*

$r_S$ = peak response of rizatriptan 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, 269.35

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

**Acceptance criteria:** 90.0%–110.0% of the labeled amount of rizatriptan

## PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

**Medium:** Water, deaerated if necessary; 900 mL

**Apparatus 2:** 50 rpm

**Time:** 15 min

Analyze the sample under test using either the *Instrumental procedure* or the *Chromatographic procedure*.

**Instrumental procedure**

**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 wavelength:** 226 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 the *Sample solution*

$A_S$ = absorbance of the *Standard solution*

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

$V$ = volume of *Medium*, 900 mL

$M_{r1}$ = molecular weight of rizatriptan, 269.35

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

$L$ = label claim of rizatriptan (mg/Tablet)

**Chromatographic procedure**

**Buffer:** 1.36 g/L of monobasic potassium phosphate. Adjust the pH of the solution with phosphoric acid to 2.5.

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

**Standard stock solution:** 0.4 mg/mL of USP Rizatriptan Benzoate RS in *Medium*

**Standard solution:** (*L*/900) mg/mL of rizatriptan from the *Standard stock solution* and *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.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 225 nm

**Column:** 4.6-mm × 15-cm; 3.5-µm packing L10

**Column temperature:** 40°

**Flow rate:** 1 mL/min

**Injection volume:** 10 µL

**Run time:** NLT 2 times the retention time of rizatriptan

**System suitability**

**Sample:** *Standard solution*

**Suitability requirements**

**Tailing factor:** NMT 2.0 for the rizatriptan peak

**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 ($C_{15}H_{19}N_5$) dissolved:

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

$r_U$ = peak response of rizatriptan from the *Sample solution*

$r_S$ = peak response of rizatriptan from the *Standard solution*

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

$V$ = volume of *Medium*, 900 mL

$M_{r1}$ = molecular weight of rizatriptan, 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.

• **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 solution:** A solution containing rizatriptan, benzoic acid, and rizatriptan *N*-oxide prepared as follows. Rinse a suitable flask with hydrogen peroxide. Heat the flask in an oven at 60° for about 10 min. Allow the flask to cool and rinse with water. Transfer 5 mL of the *Standard solution*. Add 0.2 mL of hydrogen peroxide. 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.]

**Sensitivity solution:** 0.06 µg/mL of USP Rizatriptan Benzoate RS from *Standard solution* and water

**System suitability**

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

**Suitability requirements**

**Resolution:** NLT 2.0 between benzoic acid and rizatriptan *N*-oxide, *System suitability solution*

**Tailing factor:** NMT 3 for the rizatriptan peak, *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:

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

$r_U$ = peak response of each individual degradation product

$r_T$ = sum of peak responses of rizatriptan and all degradation products excluding benzoic acid and process impurities

**Acceptance criteria:** See *Table 1*. Disregard any impurity less than 0.1%.

**Table 1**

| Name | Relative Retention Time | Acceptance Criteria, (%) |
|---|---|---|
| Benzoic acid[a] | 0.3 | — |
| Rizatriptan *N*-oxide[b] | 0.44 | 0.5 |
| Rizatriptan | 1.0 | — |
| Any individual unspecified degradation product | — | 0.2 |
| Total degradation products[c] | — | 0.75 |

[a] Not an impurity; counter ion of the drug substance, included for information only.

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

[c] Do not include benzoic acid or any known process impurities.

**ADDITIONAL REQUIREMENTS**

- **Packaging and Storage:** Preserve in well-closed, light-resistant containers. Store at controlled room temperature.
- **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 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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