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Ritonavir Tablets

DEFINITION

Ritonavir Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of ritonavir ($C_{37}H_{48}N_6O_5S_2$).

IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

• PROCEDURE

Buffer: 4.1 g/L of monobasic potassium phosphate

Solution A: Acetonitrile and *Buffer* (50:50)

Solution B: Acetonitrile, butyl alcohol, water, and *Buffer* (65:15:10:10)

Mobile phase: Acetonitrile, methanol, tetrahydrofuran (stabilizer-free), and *Buffer* (17.5:10:10:62.5). Filter the required solutions individually before use.

Standard solution: 0.1 mg/mL of [USP Ritonavir RS](#) in *Solution A*

Sample stock solution: Nominally 1 mg/mL of ritonavir prepared as follows. Transfer Tablets (NLT 5) equivalent to 500 mg of ritonavir into a 500-mL volumetric flask. Fill the flask half full with *Solution B*, and mechanically shake for at least 60 min or until the Tablets have visually disintegrated. Dilute with *Solution B* to volume, and stir for 30 min. Transfer a sufficient quantity of this solution to a centrifuge tube, and centrifuge for about 15 min. Use the supernatant to prepare the *Sample solution*.

Sample solution: Nominally 0.1 mg/mL of ritonavir in *Solution A* from the supernatant of *Sample stock solution*

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 215 nm

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

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 50 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Capacity factor: 15–24

Tailing factor: 0.8–1.2

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ritonavir ($C_{37}H_{48}N_6O_5S_2$) in the portion of Tablets taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Ritonavir RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Medium: 0.06 M polyoxyethylene 10 lauryl ether; 900 mL

Apparatus 2: 75 rpm

Time: 120 min

Buffer: 4.1 g/L of monobasic potassium phosphate

Mobile phase: Acetonitrile and *Buffer* (55:45). Adjust with phosphoric acid to a pH of 4.0 ± 0.1 .

Standard stock solution: 1.11 mg/mL of [USP Ritonavir RS](#) in methanol

Standard working solution: 111 µg/mL of [USP Ritonavir RS](#) in *Medium* from *Standard stock solution*

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

(See [Chromatography \(621\)](#), *System Suitability*.)

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 25 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: 0.9–1.5

Capacity factor: Greater than 3.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ritonavir ($C_{37}H_{48}N_6O_5S_2$) dissolved:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Ritonavir RS](#) in the *Standard solution* (mg/mL)

L = label claim for ritonavir (mg/Tablet)

V = volume of *Medium*, 900 mL

Tolerances: NLT 75% (Q) of the labeled amount of ritonavir ($C_{37}H_{48}N_6O_5S_2$) is dissolved.

• [UNIFORMITY OF DOSAGE UNITS \(905\)](#): Meet the requirements

IMPURITIES

• ORGANIC IMPURITIES

Ritonavir is alkali sensitive. All glassware should be pre-rinsed with distilled water before use to remove residual detergent contamination.

Buffer A: 4.1 g/L of monobasic potassium phosphate

Buffer B: 3.8 g/L of monobasic potassium phosphate and 0.25 g/L of dibasic potassium phosphate

Solution A: Acetonitrile and *Buffer A* (50:50)

Solution B: Acetonitrile, butyl alcohol, water, and *Buffer A* (65:15:10:10)

Solution C: Acetonitrile, butyl alcohol, and *Buffer A* (15:5:80)

Mobile phase: Acetonitrile, butyl alcohol, tetrahydrofuran (stabilizer-free), and *Buffer B* (18:5:8:69) adjusted with 1 M phosphoric acid or 1 M potassium hydroxide, if necessary, to an apparent pH of 6.3 ± 0.1

Cleaning solution: Acetonitrile, butyl alcohol, tetrahydrofuran (stabilizer-free), and *Buffer A* (30:8:13:49)

Standard stock solution: 0.05 mg/mL of [USP Ritonavir RS](#) in *Solution A*

Standard solution: 2.5 µg/mL of [USP Ritonavir RS](#) in *Solution C* from *Standard stock solution*

System suitability stock solution: 1 mg/mL of [USP Ritonavir Related Compounds Mixture RS](#) in *Solution B*



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