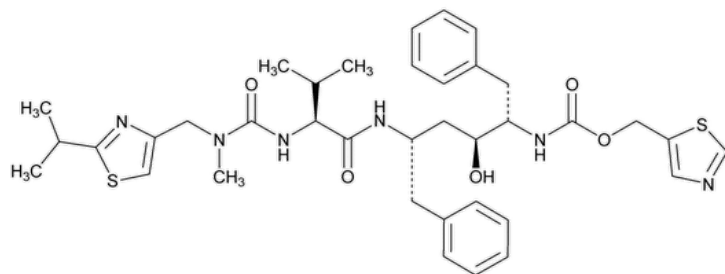


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Ritonavir



$C_{37}H_{48}N_6O_5S_2$ 720.94

2,4,7,12-Tetraazatridecan-13-oic acid, 10-hydroxy-2-methyl-5-(1-methylethyl)-1-[2-(1-methylethyl)-4-thiazolyl]-3,6-dioxo-8,11-bis(phenylmethyl)-5-thiazolylmethyl ester [5S-(5*R**,8*R**,10*R**,11*R**)]-;
 5-Thiazolylmethyl [(α S)- α -[(1*S*,3*S*)-1-hydroxy-3-[(2*S*)-2-[3-[(2-isopropyl-4-thiazolyl)methyl]-3-methylureido]3-methylbutyramido]-4-phenylbutyl]phenethyl]carbamate CAS RN®: 155213-67-5; UNII: O3J8G9O825.

DEFINITION

Ritonavir contains NLT 97.0% and NMT 102.0% of ritonavir ($C_{37}H_{48}N_6O_5S_2$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

- **A.** [▲ SPECTROSCOPIC IDENTIFICATION TESTS \(197\), Infrared Spectroscopy: 197K ▲](#) (CN 1-MAY-2020)
- **B.** The retention time of the major peak of the *Sample solution* is within 2% of the retention time of the major peak of the *Standard solution*, as obtained in the Assay.

ASSAY

PROCEDURE

Solution A: 4.1 mg/mL of monobasic potassium phosphate in water

Solution B: Acetonitrile, tetrahydrofuran (inhibitor-free), *n*-butanol, and *Solution A* (18:8:5:69)

Mobile phase: *Solution B*

Diluent: Acetonitrile and *Solution A* (1:1)

Standard stock solution: 2.0 mg/mL of [USP Ritonavir RS](#) in *Diluent*. [NOTE—This solution may be kept for 5 days if refrigerated.]

Standard solution 1: 0.10 mg/mL of [USP Ritonavir RS](#) from the *Standard stock solution* diluted with *Diluent*

Standard solution 2: 0.025 mg/mL of [USP Ritonavir RS](#) from *Standard solution 1* diluted with *Diluent*

Sample solution: 0.025 mg/mL of Ritonavir in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 15-cm; 3- μ m packing L26

Column temperature: 60°

Flow rate: 1 mL/min

Injection volume: 50 μ L

Run time: 40 min

System suitability

Sample: *Standard solution 2*

Suitability requirements

Capacity factor, k' : NLT 13

Column efficiency: NLT 5000 theoretical plates

Tailing factor: 0.8–1.2

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution 2* and *Sample solution*

Calculate the percentage of ritonavir ($C_{37}H_{48}N_6O_5S_2$) in the portion of Ritonavir 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 *Standard solution 2* (mg/mL)

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

Acceptance criteria: 97.0%–102.0% on the anhydrous basis

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.2%, determined on 1.0 g

• **ORGANIC IMPURITIES**

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

Solution A, Solution B, Mobile phase, Diluent, Standard stock solution, and Standard solution 1: Prepare as directed in the Assay.

Solution C: Acetonitrile, tetrahydrofuran (inhibitor-free), *n*-butanol, and *Solution A* (47:8:5:40)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution B (%)	Solution C (%)
0	100	0
60	100	0
120	0	100
120.1	100	0
155	100	0

Identity solution: 1 mg/mL of [USP Ritonavir Related Compounds Mixture RS](#) in *Diluent*

Standard solution 2: 5 µg/mL of [USP Ritonavir RS](#) from *Standard solution 1* in *Diluent*. [NOTE—This is stable for 48 h.]

Sample solution: 1 mg/mL of Ritonavir in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 15-cm; 3-µm packing L26

Column temperature: 60°

Flow rate: 1 mL/min

Injection volume: 50 µL

Run time

Standard solution 2: 40 min

System suitability

Samples: *Identity solution* and *Standard solution 2*

[NOTE—See [Table 2](#) for relative retention times.]