

Status: Currently Official on 15-Feb-2025
 Official Date: Official as of 01-Aug-2013
 Document Type: USP Monographs
 DocId: GUID-E746E5FA-185E-478F-AF18-A2C89BF59133_1_en-US
 DOI: https://doi.org/10.31003/USPNF_M2111_01_01
 DOI Ref: 165th

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Lopinavir and Ritonavir Tablets

DEFINITION

Lopinavir and Ritonavir Tablets contain NLT 90.0% and NMT 110.0% of the labeled amounts of lopinavir ($C_{37}H_{48}N_4O_5$) and ritonavir ($C_{37}H_{48}N_6O_5S_2$).

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.

ASSAY

• LOPINAVIR AND RITONAVIR

Buffer 1: 4.1 g/L of monobasic potassium phosphate in water

Solution A: Acetonitrile and *Buffer 1* (50:50)

Buffer 2: 2.1 g/L of monobasic potassium phosphate in water

Solution B: Acetonitrile and 1-butanol (13:3)

Solution C: Acetonitrile, 1-butanol, *Buffer 1*, and water (65:15:10:10)

Standard solution: 6.25 µg/mL of [USP Ritonavir RS](#) and 25 µg/mL of [USP Lopinavir RS](#) in *Solution A*

Sample solution: Place a number of Tablets equivalent to 1000 mg of lopinavir and 250 mg of ritonavir in a 250-mL volumetric flask, add 25 mL of *Buffer 2*, and agitate to dissolve the Tablet coating, if necessary. Add 100 mL of *Solution B*, and shake mechanically until the Tablets are dissolved. Dilute with *Solution C* to volume. Centrifuge a portion of this solution, and then further dilute with *Solution A* to a nominal concentration of 6.25 µg/mL of ritonavir and 25 µg/mL of lopinavir.

Mobile phase: Acetonitrile, methanol, tetrahydrofuran, and *Buffer 1* (175:100:100:625)

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*

[NOTE—The elution order is ritonavir, then lopinavir.]

Suitability requirements

Capacity factor: 15–24 for the ritonavir peak

Tailing factor: 0.8–1.2 for the ritonavir peak

Theoretical plates: More than 5000 for the ritonavir peak

Relative standard deviation: NMT 2.0% for the ritonavir and lopinavir peaks

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lopinavir ($C_{37}H_{48}N_4O_5$) and 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 of lopinavir or ritonavir from the *Sample solution*

r_S = peak response of lopinavir or ritonavir from the *Standard solution*

C_s = concentration of lopinavir or ritonavir in the *Standard solution* ($\mu\text{g/mL}$)

C_u = nominal concentration of lopinavir or ritonavir in the *Sample solution* ($\mu\text{g/mL}$)

Acceptance criteria: 90.0%–110.0% of the labeled amounts of lopinavir ($\text{C}_{37}\text{H}_{48}\text{N}_4\text{O}_5$) and ritonavir ($\text{C}_{37}\text{H}_{48}\text{N}_6\text{O}_5\text{S}_2$)

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Medium: 60 mM polyoxyethylene 10 lauryl ether (37.56 g/L) in water; 900 mL

Apparatus 2: 75 rpm

Time: 90 min

Mobile phase: Acetonitrile and 4.1 g/L potassium phosphate monobasic (55:45). Adjust with phosphoric acid to an apparent pH of 4.0 ± 0.05 .

Standard solution: Dissolve [USP Lopinavir RS](#) in methanol to obtain a solution containing 2.6 mg/mL. Dissolve [USP Ritonavir RS](#) in methanol to obtain a solution containing 1.3 mg/mL. Combine portions of these solutions to make a solution containing approximately 0.104 mg/mL of lopinavir and 0.026 mg/mL of ritonavir in *Medium*.

Sample solutions: Pass a portion of the solution under test through a suitable filter. If necessary, dilute the solution with *Medium* to obtain a final sample solution containing approximately 0.104 mg/mL of lopinavir and 0.026 mg/mL of ritonavir.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm $\times$ 15-cm; 5- μm packing L1

Flow rate: 1.5 mL/min

Injection volume: 25 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between lopinavir and ritonavir

Tailing factor: 0.9–1.5 for the lopinavir and ritonavir peaks

Relative standard deviation: NMT 2.0% for the lopinavir and ritonavir peaks

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of lopinavir ($\text{C}_{37}\text{H}_{48}\text{N}_4\text{O}_5$) and ritonavir ($\text{C}_{37}\text{H}_{48}\text{N}_6\text{O}_5\text{S}_2$) dissolved:

$$\text{Result} = (r_u/r_s) \times (C_s/L) \times D \times V \times 100$$

r_u = peak response of lopinavir or ritonavir from the *Sample solution*

r_s = peak response of lopinavir or ritonavir from the *Standard solution*

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

L = Tablet label claim for lopinavir or ritonavir (mg)

D = dilution factor of the *Sample solution*

V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (Q) of the labeled amounts of lopinavir ($\text{C}_{37}\text{H}_{48}\text{N}_4\text{O}_5$) and ritonavir ($\text{C}_{37}\text{H}_{48}\text{N}_6\text{O}_5\text{S}_2$) are dissolved.

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

IMPURITIES

• ORGANIC IMPURITIES

Buffer 1: 4.1 g/L of monobasic potassium phosphate in water

Solution A: *Buffer 1* and acetonitrile (50:50)

Buffer 2: 2.1 g/L of monobasic potassium phosphate in water

Solution B: Acetonitrile, 1-butanol, and *Buffer 1* (15:5:80)

Solution C: Acetonitrile, 1-butanol, *Buffer 1*, and water (65:15:10:10)

Solution D: Acetonitrile and 1-butanol (13:3)