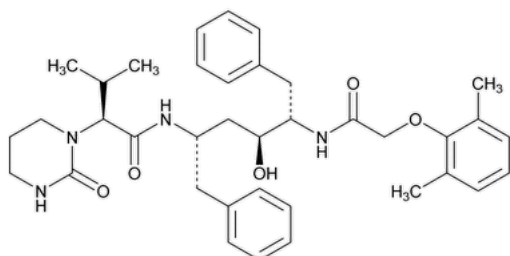


Status: Currently Official on 15-Feb-2025
 Official Date: Official as of 01-May-2020
 Document Type: USP Monographs
 DocId: GUID-EE0CBB31-5FC4-4D04-AFEA-A8B29C690822_4_en-US
 DOI: https://doi.org/10.31003/USPNF_M45872_04_01
 DOI Ref: o3bg6

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Lopinavir



$C_{37}H_{48}N_4O_5$

628.80

[1S-[1*R**(*R**),3*R**,4*R**]]-N-[4[[[2,6-Dimethylphenoxy] acetyl]amino]-3-hydroxy-5-phenyl-1-(phenylmethyl)pentyl]-tetrahydro- α -(1-methylethyl)-2-oxo-1(2*H*)-pyrimidineacetamide;

(α S)-Tetrahydro-N-[(α S)- α -[(2*S*,3*S*)-2-hydroxy-4-phenyl-3-[2-(2,6-xylyloxy)acetamido]butyl]phenethyl]- α -isopropyl-2-oxo-1(2*H*)-pyrimidineacetamide CAS RN®: 192725-17-0; UNII: 2494G1JF75.

DEFINITION

Lopinavir contains NLT 98.0% and NMT 102.0% of lopinavir ($C_{37}H_{48}N_4O_5$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

- A. ▲ **SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy: 197A** ▲ (CN 1-MAY-2020)
- B. The retention time of the lopinavir peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

PROCEDURE

Buffer: 2.7 g/L of monobasic potassium phosphate and 0.9 g/L of dibasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 6.0. Pass the solution through a suitable filter of 0.45- μ m pore size.

Diluent: Acetonitrile and water (1:1)

Solution A: Acetonitrile and *Buffer* (9:11)

Mobile phase: *Solution A*

Standard solution: 0.025 mg/mL of [USP Lopinavir RS](#) in *Diluent*

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

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm $\times$ 25-cm; 4- μ m packing L1

Column temperature: 50°

Flow rate: 1 mL/min

Injection volume: 20 μ L

Run time: 60 min

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 8000 theoretical plates

Capacity factor: NLT 15

Tailing factor: 0.8–1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of lopinavir ($C_{37}H_{48}N_4O_5$) in the portion of Lopinavir 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 Lopinavir RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

• **RESIDUE ON IGNITION (281):** NMT 0.2%

• **ORGANIC IMPURITIES: PROCEDURE 1**

[NOTE—For early-eluting impurities.]

Buffer, Diluent, and Solution A: Prepare as directed in the Assay.

Solution B: Acetonitrile and *Buffer* (3:1)

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

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
60	100	0
61	0	100
81	0	100
82	100	0
100	100	0

System suitability solution: 0.5 mg/mL of [USP Lopinavir System Suitability Mixture RS](#) in *Diluent*

Standard solution: 0.005 mg/mL of [USP Lopinavir RS](#) in *Diluent*

Sample solution: 0.5 mg/mL of Lopinavir in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 4-μm packing L1

Column temperature: 50°

Flow rate: 1 mL/min

Injection volume: 20 μL

Run time: 100 min

[NOTE—Data collection is only for the first 60 min. The remaining gradient steps wash out the late-eluting impurities and re-equilibrate the column.]

System suitability

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

[NOTE—The relative retention times are listed in [Table 2](#).]

Suitability requirements

Resolution: NLT 1.2 between lopinavir *N*-formylphenoxyacetamide and lopinavir *N*-acetylphenoxyacetamide, *System suitability solution*

Capacity factor: NLT 15, *Standard solution*

Column efficiency: NLT 8000, *Standard solution*

Tailing factor: 0.8–1.5, *Standard solution*

Relative standard deviation: NMT 3.0%, *Standard solution*

Analysis

Samples: *Diluent*, *System suitability solution*, *Standard solution*, and *Sample solution*

Calculate the percentage of each lopinavir related impurity and unidentified impurity in the portion of Lopinavir taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$