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Lopinavir and Ritonavir Oral Solution

DEFINITION

Lopinavir and Ritonavir Oral Solution contains 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 lopinavir and ritonavir peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Lopinavir and Ritonavir**

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

Solution A: Acetonitrile and *Buffer* (65:35)

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

Mobile phase: Acetonitrile, methanol, tetrahydrofuran, and *Buffer* (175:100:100:625). Separately filter the *Buffer* and the premixed solvents before combining them to make the *Mobile phase*.

Standard stock solution: 0.1 mg/mL each of USP Lopinavir RS and USP Ritonavir RS in *Solution B*

Standard solution: 0.025 mg/mL each of USP Lopinavir RS and USP Ritonavir RS in *Solution B* from the *Standard stock solution*

Sample stock solution: Nominally 4 mg/mL of lopinavir and 1 mg/mL of ritonavir in *Solution A* prepared as follows. Transfer a volume of Oral Solution equivalent to 400 mg of lopinavir and 100 mg of ritonavir to a 100-mL volumetric flask with the aid of several small portions of *Solution A*, and then dilute with *Solution A* to volume.

Sample solution: Nominally 0.05 mg/mL of lopinavir and 0.0125 mg/mL of ritonavir in *Solution B* from the *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

Tailing factor: 0.8–1.2 for the ritonavir peak

Relative standard deviation: NMT 2.0% each for ritonavir and lopinavir

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentages of the labeled amounts of lopinavir ($C_{37}H_{48}N_4O_5$) and ritonavir ($C_{37}H_{48}N_6O_5S_2$) in the portion of Oral Solution taken:

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

r_U = peak response of the corresponding analyte from the *Sample solution*

r_S = peak response of the corresponding analyte from the *Standard solution*

C_S = concentration of USP Lopinavir RS or USP Ritonavir RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0% of the labeled amounts of lopinavir ($C_{37}H_{48}N_4O_5$) and ritonavir ($C_{37}H_{48}N_6O_5S_2$)

PERFORMANCE TESTS

• **Deliverable Volume ⟨698⟩**

For multiple-unit containers

Acceptance criteria: Meets the requirements

IMPURITIES

• **Organic Impurities**

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

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

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

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

Solution C: Acetonitrile and *Buffer A* (65:35)

Mobile phase: Acetonitrile, tetrahydrofuran, butyl alcohol, and *Buffer B* (18:8:5:69). Adjust with 1 M phosphoric acid or 1 M potassium hydroxide, if necessary, to a pH of 6.3.

Standard stock solution: 0.1 mg/mL each of USP Lopinavir RS and USP Ritonavir RS in *Solution A*

Standard solution: 0.01 mg/mL each of USP Lopinavir RS and USP Ritonavir RS from *Standard stock solution* in *Solution B*

Peak identification solution: Transfer a weighed portion of Oral Solution to a crimp-top container. Add an amount of citric acid equivalent to 1% by weight of the Oral Solution taken and mix until dissolved. Seal the container, and heat at 50° for approximately 4 days. Use this degradation solution and follow the procedure described below in the *Sample stock solution* and *Sample solution* sections to prepare the *Peak identification solution*.

Sample stock solution: Transfer 5 mL of Oral Solution with the aid of several small portions of *Solution C* to a 100-mL volumetric flask, and dilute with *Solution C* to volume.

Sample solution: Dilute 25.0 mL of *Sample stock solution* with *Solution B* to 50.0 mL. Transfer 15.0 mL of this solution to a 50-mL centrifuge tube that has been previously rinsed with methanol and dried. Add 20.0 mL of *n*-heptane, and shake vigorously until a uniform emulsion is formed. Vent the tube periodically while shaking. Centrifuge the emulsion for about 5 min. Carefully remove the top heptane layer by aspiration, leaving the clear *Sample solution* layer. The middle viscous, cloudy layer should be considered part of the heptane layer for removal by aspiration. Precondition a strong anion-exchange cartridge (quaternary ammonium functionality on a styrene/divinylbenzene base) with a sorbent mass of 600 mg by rinsing the cartridge with 3 mL of methanol, then 3 mL of *Solution C*, and repeating these rinse steps. Dry the cartridge for about 10 min with the aid of a low vacuum. Transfer 5.0 mL of the clear *Sample solution* to the preconditioned cartridge. With the aid of a vacuum, slowly pass the *Sample solution* completely through the cartridge, collect the extract in a 5-mL volumetric flask, and then dilute with *Solution C* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm and 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: 2 times the retention time of lopinavir

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2.5 between the ritonavir and lopinavir peaks at 215 nm

Tailing factor: 0.8–1.2 for the ritonavir peak at 240 nm

Relative standard deviation: NMT 3.0% for the lopinavir peak at 215 nm; NMT 3.0% for the ritonavir peak at 240 nm

Analysis

Samples: *Standard solution*, *Peak identification solution*, and *Sample solution*

[Note—Determine the relative retention values (*r*) for the components listed in *Table 1* and *Table 2*, using the time measured at the first baseline deflection of the *Standard solution* chromatogram as the void volume (t_M).]

To identify the ritonavir impurities, determine the relative retention value from the 240-nm chromatogram relative to ritonavir (see *Table 1*). The *Peak identification solution* may also be used to identify ritonavir degradants. Unspecified ritonavir impurities are assigned

according to the algorithm outlined in *Table 3*.

Calculate the percentage of each ritonavir impurity in the portion of Oral Solution taken:

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

r_U = peak response of each individual impurity from the *Sample solution*

r_S = peak response of ritonavir 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)

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Value (*r*)	Relative Response Factor	Acceptance Criteria, NMT (%)
Ureidovaline[a]	0.03	—	—[b]
N-Deacylvaline ritonavir[c]	0.11	0.81	0.8
Glycerol carbamate analog[d]	0.14	0.62	0.2
Acetamidoalcohol[e]	0.15	—	—[b]
Hydroxypropyl carbamate analog[f]	0.24[g]	0.59	0.5
2,5-Thiazolylmethyldicarbamate[h]	0.24[i]	—	—[b]
Hydroxyritonavir[j]	0.36	0.86	0.3
Hydantoin aminoalcohol[k]	0.39	0.73	0.4
Ritonavir hydroperoxide[l]	0.44[i]	0.88	0.2
Ethyl carbamate analog[m]	0.45[i]	0.66	0.7
Hydantoin-oxazolidinone derivative[n]	0.50	—	—[b]
Ethyl analog[o]	0.64	—	—[b]
O-Acyl isomer[p]	0.74	1.1	0.2
BOC-aminoalcohol[q]	0.81	—	—[b]
Isobutoxycarbonyl aminoalcohol[r]	0.81	—	—[b]

Name	Relative Retention Value (*r*)	Relative Response Factor	Acceptance Criteria, NMT (%)
Oxazolidinone derivative[s]	0.87	0.53	0.2
Ureidovaline isobutyl ester[t]	0.94	—	—[b]
Ritonavir	1.0	—	—
4-Hydroxy isomer[u]	1.05	—	—[b]
3*R*-Epimer[v]	1.11	—	—[b]
Aminoalcohol urea derivative[w]	1.14	—	—[b]
3*R*,5*R*-Epimer[x]	1.23	—	—[b]
5*R*-Epimer[y]	1.32	—	—[b]
Diacyl valine urea[z]	1.70	—	—[b]
Any unspecified ritonavir impurity	—	1.0	0.2
Total ritonavir impurities, specified and unspecified	—	—	3.0[aa]

[a] [*N*-Methyl[(2-isopropyl-4-thiazolyl)methyl]amino]carbonyl-L-valine.

[aa] Disregard any peak less than 0.01% in the calculation of total impurities.

[b] These are process impurities which are included in this table for identification only. These impurities are controlled in the drug substance. They are not to be reported for the drug product and are not included in the total impurities.

[c] Thiazol-5-ylmethyl (2*S*,3*S*,5*S*)-5-[(*S*)-2-amino-3-methylbutanamido]-3-hydroxy-1,6-diphenylhexan-2-ylcarbamate.

[d] Thiazol-5-ylmethyl (2*S*,3*S*,5*S*)-5-[(2*S*)-2-(2,3-dihydroxypropoxycarbonylamino)-3-methylbutanamido]-3-hydroxy-1,6-diphenylhexan-2-ylcarbamate.

[e] Thiazol-5-ylmethyl (2*S*,3*S*,5*S*)-5-[(2*S*)-2-(2-hydroxypropoxycarbonylamino)-3-methylbutanamido]-3-hydroxy-1,6-diphenylhexan-2-ylcarbamate.

[f] Thiazol-5-ylmethyl (2*S*,3*S*,5*S*)-5-acetamido-3-hydroxy-1,6-diphenylhexan-2-ylcarbamate.

[g] If two peaks appear with a relative retention value of 0.24, the second peak will be identified as 2,5-thiazolylmethyldicarbamate.

[h] 2,5-Thiazolylmethyldicarbamate.

[i] A single peak with a relative retention value of 0.44 should be reported as the ethyl carbamate analog due to possible coelution with ritonavir hydroperoxide impurity.

[j] Thiazol-5-ylmethyl (2*S*,3*S*,5*S*)-3-hydroxy-5-[2-(3-{[2-(2-hydroxypropan-2-yl)thiazol-4-yl]methyl}-3-methylureido)acetamido]-1,6-diphenylhexan-2-ylcarbamate.

[k] Thiazol-5-ylmethyl (2*S*,3*S*,5*S*)-3-hydroxy-5-[(*S*)-4-isopropyl-2,5-dioxoimidazolidin-1-yl]-1,6-diphenylhexan-2-ylcarbamate.

[l] Thiazol-5-ylmethyl (2*S*,3*S*,5*S*)-5-[(*S*)-2-ethoxycarbonylamino-3-methylbutanamido]-3-hydroxy-1,6-diphenylhexan-2-ylcarbamate.

[m] Thiazol-5-ylmethyl (2*S*,3*S*,5*S*)-5-[(*S*)-2-{3-[(2-ethylthiazol-4-yl)methyl]-3-methylureido}-3-methylbutanamido]-3-hydroxy-1,6-diphenylhexan-2-ylcarbamate.

[n] (4*S*,5*S*)-Thiazol-5-ylmethyl 4-benzyl-5-{(*S*)-2-[(*S*)-4-isopropyl-2,5-dioxoimidazolidin-1-yl]-3-phenylpropyl}-2-oxooxazolidine-3-carboxylate.

[o] Thiazol-5-ylmethyl (2*S*,3*S*,5*S*)-5-[(*S*)-2-{3-[(2-ethylthiazol-4-yl)methyl]-3-methylureido}-3-methylbutanamido]-3-hydroxy-1,6-diphenylhexan-2-ylcarbamate.

[p] (*S*)-{(2*S*,3*S*,5*S*)-5-Amino-1,6-diphenyl-2-[(thiazol-5-ylmethoxy)carbonylamino]hexan-3-yl} 2-{3-[(2-isopropylthiazol-4-yl)methyl]-3-methylureido}-3-methylbutanoate.

[q] Thiazol-5-ylmethyl (2*S*,3*S*,5*S*)-(5-*t*-butoxycarbonylamino)-3-hydroxy-1,6-diphenylhexan-2-ylcarbamate.

[r] Thiazol-5-ylmethyl (2*S*,3*S*,5*S*)-(5-isobutoxycarbonylamino)-3-hydroxy-1,6-diphenylhexan-2-ylcarbamate.

[s] (*S*)-*N*-[(*S*)-1-[(4*S*,5*S*)-4-Benzyl-2-oxooxazolidin-5-yl]-3-phenylpropan-2-yl]-2-{3-[(2-isopropylthiazol-4-yl)methyl]-3-methylureido}-3-methylbutanamide.

[t] (*S*)-Isobutyl 2-{3-[(2-isopropylthiazol-4-yl)methyl]-3-methylureido}-3-methylbutanoate.

[u] Thiazol-5-ylmethyl (2*S*,4*S*,5*S*)-4-hydroxy-5-[(*S*)-2-{3-[(2-isopropylthiazol-4-yl)methyl]-3-methylureido}-3-methylbutanamido]-1,6-diphenylhexan-2-ylcarbamate.

[v] Thiazol-5-ylmethyl (2*S*,3*R*,5*S*)-3-hydroxy-5-[(*S*)-2-{3-[(2-isopropylthiazol-4-yl)methyl]-3-methylureido}-3-methylbutanamido]-1,6-diphenylhexan-2-ylcarbamate.

[w] Bis(thiazol-5-ylmethyl) (2*S*,2'*S*,3*S*,3'*S*,5*S*,5'*S*)-5,5'-carbonylbis(azanediyl)bis(3-hydroxy-1,6-diphenylhexane-5,2-diyl)dicarbamate.

[x] Thiazol-5-ylmethyl (2*S*,3*R*,5*R*)-3-hydroxy-5-[(*S*)-2-{3-[(2-isopropylthiazol-4-yl)methyl]-3-methylureido}-3-methylbutanamido]-1,6-diphenylhexan-2-ylcarbamate.

[y] Thiazol-5-ylmethyl (2*S*,3*S*,5*R*)-3-hydroxy-5-[(*S*)-2-{3-[(2-isopropylthiazol-4-yl)methyl]-3-methylureido}-3-methylbutanamido]-1,6-diphenylhexan-2-ylcarbamate.

[z] (*S*)-*N*-[(2*S*,4*S*,5*S*)-5-(Thiazol-5-ylmethoxycarbonylamino)-4-hydroxy-1,6-diphenylhexan-2-yl]-2-{3-[(2*S*,4*S*,5*S*)-5-(thiazol-5-ylmethoxycarbonylamino)-4-hydroxy-1,6-diphenylhexan-2-yl]ureido}-3-methylbutanamide.

To identify the lopinavir impurities, determine the relative retention value from the 215-nm chromatogram relative to ritonavir (see *Table 2*). Compare the 215-nm chromatogram to the 240-nm chromatogram. Any impurity assigned as a ritonavir impurity at 240 nm that is also observed at 215 nm is discounted. Unspecified ritonavir impurities are assigned according to the algorithm outlined in *Table 3*.

Calculate the percentage of each unspecified lopinavir impurity at 215 nm in the portion of Oral Solution taken:

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

r_U = peak response of each individual impurity from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Value (*r*)	Acceptance Criteria, NMT (%)
Lopinavir aminoalcohol[a]	0.06	—[b]
Lopinavir *N*-formylaminoalcohol[c]	0.12	—[b]
Lopinavir divalinate[d]	0.21	—[b]
Lopinavir phenoxyacetamide[e]	0.35	—[b]
Lopinavir *N*-formylphenoxyacetamide[f]	0.67	—[b]
Lopinavir *N*-acetylphenoxyacetamide[g]	0.69	—[b]
Lopinavir oxazine[h]	0.77	—[b]

Name	Relative Retention Value (*r*)	Acceptance Criteria, NMT (%)
Z-Diacylethenediamine[i]	0.92	—[b]
Ritonavir	1.0	—[b]
Isolopinavir[j]	1.18	—[b]
Lopinavir 2,4-dimethylphenoxy isomer[k]	1.21	—[b]
Lopinavir 4-epimer[l]	1.26	—[b]
Lopinavir D-valine diastereomer[m]	1.33	—[b]
Lopinavir (2*R*,4*R*) diastereomer[n]	1.42	—[b]
Lopinavir 2-epimer[o]	1.79	—[b]
Any unspecified lopinavir impurity	—	0.2[p]
Total unspecified lopinavir impurities	—	0.5[p]

[a] (*S*)-*N*-[(2*S*,4*S*,5*S*)-5-Amino-4-hydroxy-1,6-diphenylhexan-2-yl]-3-methyl-2-[2-oxotetrahydropyrimidin-1(2*H*)-yl]butanamide.

[b] These are process impurities which are included in this table for identification only. These impurities are controlled in the drug substance. They are not to be reported for the drug product and are not included in the total impurities.

[c] (*S*)-*N*-[(2*S*,4*S*,5*S*)-5-Formamido-4-hydroxy-1,6-diphenylhexan-2-yl]-3-methyl-2-[2-oxotetrahydropyrimidin-1(2*H*)-yl]butanamide.

[d] (2*S*,2′*S*)-*N*,*N*′-[(2*S*,3*S*,5*S*)-3-Hydroxy-1,6-diphenylhexane-2,5-diyl]bis{3-methyl-2-[2-oxotetrahydropyrimidin-1(2*H*)-yl]butanamide}.

[e] *N*-[(2*S*,3*S*,5*S*)-5-Amino-3-hydroxy-1,6-diphenylhexan-2-yl]-2-(2,6-dimethylphenoxy)acetamide.

[f] 2-(2,6-Dimethylphenoxy)-*N*-[(2*S*,3*S*,5*S*)-5-formamido-3-hydroxy-1,6-diphenylhexan-2-yl]acetamide.

[g] *N*-[(2*S*,3*S*,5*S*)-5-Acetamido-3-hydroxy-1,6-diphenylhexan-2-yl]-2-(2,6-dimethylphenoxy)acetamide.

[h] *N*-{(*S*)-1-[(4*S*,6*S*)-4-Benzyl-2-oxo-1,3-oxazinan-6-yl]-2-phenylethyl}-2-(2,6-dimethylphenoxy)acetamide.

[i] (*Z*)-*N*,*N*′-(Ethene-1,2-diyl)bis[2-(2,6-dimethylphenoxy)acetamide].

[j] (*S*)-*N*-{(2*S*,3*S*,5*S*)-5-[2-(2,6-Dimethylphenoxy)acetamido]-3-hydroxy-1,6-diphenylhexan-2-yl}-3-methyl-2-[2-oxotetrahydropyrimidin-1(2*H*)-yl]butanamide.

[k] (*S*)-*N*-{(2*S*,4*S*,5*S*)-5-[2-(2,4-Dimethylphenoxy)acetamido]-4-hydroxy-1,6-diphenylhexan-2-yl}-3-methyl-2-[2-oxotetrahydropyrimidin-1(2*H*)-yl]butanamide.

[l] (*S*)-*N*-{(2*S*,4*R*,5*S*)-5-[2-(2,6-Dimethylphenoxy)acetamido]-4-hydroxy-1,6-diphenylhexan-2-yl}-3-methyl-2-[2-oxotetrahydropyrimidin-1(2*H*)-yl]butanamide.

[m] (*R*)-*N*-{(2*S*,4*S*,5*S*)-5-[2-(2,6-Dimethylphenoxy)acetamido]-4-hydroxy-1,6-diphenylhexan-2-yl}-3-methyl-2-[2-oxotetrahydropyrimidin-1(2*H*)-yl]butanamide.

[n] (*S*)-*N*-{(2*R*,4*R*,5*S*)-5-[2-(2,6-Dimethylphenoxy)acetamido]-4-hydroxy-1,6-diphenylhexan-2-yl}-3-methyl-2-[2-oxotetrahydropyrimidin-1(2*H*)-yl]butanamide.

[o] (*S*)-*N*-{(2*R*,4*S*,5*S*)-5-[2-(2,6-Dimethylphenoxy)acetamido]-4-hydroxy-1,6-diphenylhexan-2-yl}-3-methyl-2-[2-oxotetrahydropyrimidin-1(2*H*)-yl]butanamide.

[p] Disregard any peak less than 0.01%.

For calculating and reporting impurities, follow the algorithm outlined in *Table 3*.

Table 3

Wavelength (nm)	Unspecified Impurity Observed	
240	Yes	No
215	Yes or No	Yes
Peak assigned to	Ritonavir	Lopinavir
Quantitation wavelength	240 nm	215 nm

SPECIFIC TESTS

• **Alcohol Determination ⟨611⟩**

Internal standard solution: Transfer 10.0 mL of butyl alcohol to a 200-mL volumetric flask and dilute with methanol to volume.

Internal standard identification solution: Dilute 5.0 mL of *Internal standard solution* with methanol to 100 mL.

Standard stock solution: 4.0% (v/v) of dehydrated alcohol in methanol

Standard solution: 0.4% (v/v) of dehydrated alcohol prepared as follows. Transfer 10.0 mL of *Standard stock solution* and 5.0 mL of the *Internal standard solution* to a 100-mL volumetric flask, and dilute with methanol to volume.

Sample stock solution: Transfer 5.0 mL of Oral Solution to a 50-mL volumetric flask with the aid of several portions of methanol, and dilute with methanol to volume.

Sample solution: Transfer 10.0 mL of *Sample stock solution* and 5.0 mL of the *Internal standard solution* to a 100-mL volumetric flask, and dilute with methanol to volume.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.53-mm × 30-m fused silica capillary; coated with a 1-µm film of liquid phase G16

Temperatures

Injection port: 185°

Detector: 220°

Column: See *Table 4*.

Table 4

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
40	0	40	5
40	10	145	6
145	20	200	9.75

Carrier gas: Helium

Flow rate: 4.5 mL/min

Makeup gas flow: 30 mL/min

Injection volume: 1 µL

Injection type: Split ratio 4:1

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: 0.8–1.2 for the alcohol peak

Relative standard deviation: NMT 3.0% for the peak area ratio of alcohol to the internal standard

Analysis

Samples: *Internal standard identification solution*, *Standard solution*, and *Sample solution*

Calculate the percentage of the labeled amount of alcohol in the portion of Oral Solution taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times D \times 100$$

R_U = peak response ratio of alcohol to butyl alcohol from the *Sample solution*

R_S = peak response ratio of alcohol to butyl alcohol from the *Standard solution*

C_S = concentration of dehydrated alcohol in the *Standard solution* (% v/v)

C_U = nominal concentration of alcohol in the Oral Solution (% v/v)

D = dilution factor used to prepare the *Sample solution*

Acceptance criteria: 85.0%–115.0% of the labeled amount of alcohol (C_2H_6O)

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count does not exceed 10^2 cfu/mL.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers, protected from light. Store at 2°–8°.

• **USP Reference Standards ⟨11⟩**

USP Lopinavir RS

USP Ritonavir RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
LOPINAVIR AND RITONAVIR ORAL SOLUTION	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

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