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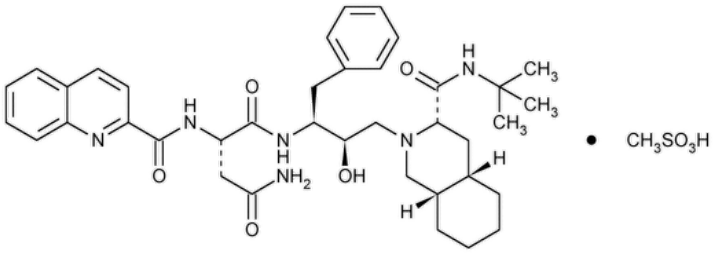
Saquinavir Mesylate

Change to read:



$C_{38}H_{50}N_6O_5 \cdot CH_4O_3S$ ▲766.96▲ (USP 1-Dec-2022)

Butanediamide, *N*[1]-[3-[3-[[(1,1-dimethylethyl)amino]carbonyl]octahydro-2(1*H*)-isoquinolinyl]-2-hydroxy-1-(phenylmethyl)propyl]-2-[(2-quinolinylcarbonyl)amino]-, [3*S*-[2[1*R**(*R**),2*S**],3α,4aβ,8aβ]]-, monomethanesulfonate (salt);
(*S*)-*N*-[(α*S*)-α-[(1*R*)-2-[(3*S*,4a*S*,8a*S*)-3-(*tert*-Butylcarbamoyl)octahydro-2(1*H*)-isoquinolyl]-1-hydroxyethyl]phenethyl]-2-quinaldamidosuccinamide monomethanesulfonate (salt) CAS RN®: 149845-06-7; UNII: UHB9Z3841A.

DEFINITION
Saquinavir Mesylate contains NLT 98.5% and NMT 101.0% of saquinavir mesylate ($C_{38}H_{50}N_6O_5 \cdot CH_4O_3S$), calculated on the anhydrous basis.

IDENTIFICATION
Change to read:

• **A.** **Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K ▲or 197A▲ (USP 1-Dec-2022)

Delete the following:

▲• **B.** **Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*▲** (USP 1-Dec-2022)

Change to read:

• **▲B.▲** (USP 1-Dec-2022) The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
Change to read:

• **Procedure**

Buffer: Transfer 10 mL of triethylamine to a 1 L flask, and dilute with water to volume. Adjust with phosphoric acid to a pH of 2.5.

Mobile phase: Acetonitrile, tetrahydrofuran, and *Buffer* (5:25:70). [Note—Protect from light.]

System suitability solution: 0.25 mg/mL of USP Saquinavir Mesylate RS and 0.002 mg/mL of USP Saquinavir Related Compound A RS in *Mobile phase*

Standard solution: 0.25 mg/mL of USP Saquinavir Mesylate RS in *Mobile phase*

Sample solution: 0.25 mg/mL of Saquinavir Mesylate in *Mobile phase*, and mix for about 20 min

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; packing L1

Column temperature: 20°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

[NOTE—The relative retention times for saquinavir related compound A and saquinavir are 0.89 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between saquinavir related compound A and saquinavir, *System suitability solution*

▲**Tailing factor:** NMT 2.0, *Standard solution*▲ (USP 1-Dec-2022)

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of saquinavir mesylate ($C_{38}H_{50}N_6O_5 \cdot CH_4O_3S$) in the portion of Saquinavir Mesylate taken:

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

r_U = peak response of saquinavir from the *Sample solution*

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

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

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

Acceptance criteria: 98.5%–101.0% on the anhydrous basis

IMPURITIES

• **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%

Change to read:

• **ORGANIC IMPURITIES**

Buffer, Mobile phase, System suitability solution, Standard solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

▲**Sensitivity solution:** 0.125 µg/mL of USP Saquinavir Mesylate RS in *Mobile phase*▲ (USP 1-Dec-2022)

System suitability

Samples: *System suitability solution*, *Standard solution*, ▲and *Sensitivity solution*▲ (USP 1-Dec-2022)

[NOTE—The relative retention times for saquinavir related compound A and saquinavir are 0.89 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between saquinavir related compound A and saquinavir, *System suitability solution*

▲**Tailing factor:** NMT 2.0, *Standard solution*▲ (USP 1-Dec-2022)

Relative standard deviation: NMT 2.0%, *Standard solution*

▲**Signal-to-noise-ratio:** NLT 10, *Sensitivity solution*▲ (USP 1-Dec-2022)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual impurity in the portion of Saquinavir Mesylate taken:

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

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

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

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

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

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

▲**Acceptance criteria:** See *Table 1*. The reporting threshold is 0.05%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Saquinavir amine[a]	0.32	0.5	0.1
Quinolinoyl asparagine[b]	0.38	2.0	0.1
Ethyl quinolinoyl asparagine[c]	0.53	2.0	0.1
Saquinavir	1.0	—	—
Any individual unspecified impurity	—	1.0	0.1
Total impurities	—	—	0.5▲ (USP 1-Dec-2022)

[a] (3*S*,4a*S*,8a*S*)-2-[(2*R*,3*S*)-3-Amino-2-hydroxy-4-phenylbutyl]-*N*-(*tert*-butyl)decahydroisoquinoline-3-carboxamide.

[b] (Quinoline-2-carbonyl)-L-asparagine.

[c] Ethyl (quinoline-2-carbonyl)-L-asparaginate.

SPECIFIC TESTS

• **Optical Rotation** ⟨781S⟩, *Procedures*, *Specific Rotation*

Sample solution: 5 mg/mL in methanol

Acceptance criteria: −66.8° to −69.6° (λ = 436 nm at 20°)

• **Water Determination** ⟨921⟩, *Method I*: NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Saquinavir Mesylate RS

USP Saquinavir Related Compound A RS

▲N^1-{(2*S*,3*R*)-3-Hydroxy-4-[(3*S*,4a*S*,8a*S*)-3-[(2-methyl-2-propanyl)carbamoyl]octahydro-2(1*H*)-isoquinolinyl]-1-phenylbutan-2-yl}-N^2-(quinoline-2-carbonyl)-D-asparaginamide.▲ (USP 1-Dec-2022)

$C_{38}H_{50}N_6O_5$ ▲670.86▲ (USP 1-Dec-2022)

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

Topic/Question	Contact	Expert Committee
SAQUINAVIR MESYLATE	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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