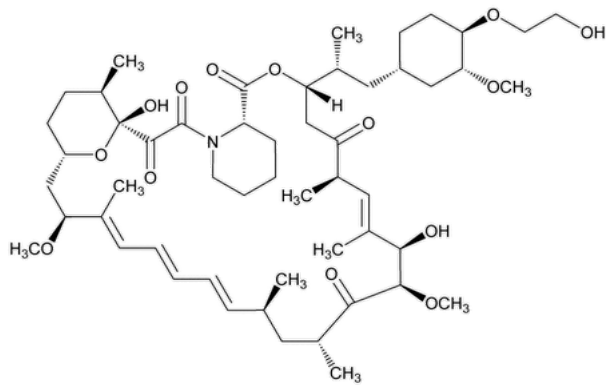


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Everolimus

Change to read:



$C_{53}H_{83}NO_{14}$ Δ 958.24 Δ (CN 1-Aug-2024)
(1*R*,9*S*,12*S*,15*R*,16*E*,18*R*,19*R*,21*R*,23*S*,24*E*,26*E*,28*E*,30*S*,32*S*,35*R*)-1,18-Dihydroxy-12-[(1*R*)-2-[(1*S*,3*R*,4*R*)-4-(2-hydroxyethoxy)-3-methoxycyclohexyl]-1-methylethyl]-19,30-dimethoxy-15,17,21,23,29,35-hexamethyl-11,36-dioxo-4-azatricyclo[30.3.1.0^{4,9}]hexatriaconta-16,24,26,28-tetraene-2,3,10,14,20-pentaone;
(3*S*,6*R*,7*E*,9*R*,10*R*,12*R*,14*S*,15*E*,17*E*,19*E*,21*S*,23*S*,26*R*,27*R*,34*aS*)-9,10,12,13,14,21,22,23,24,25,26,27,32,33,34,34*a*-Hexadecahydro-9,27-dihydroxy-3-[(1*R*)-2-[(1*S*,3*R*,4*R*)-4-(2-hydroxyethoxy)-3-methoxycyclohexyl]-1-methylethyl]-10,21-dimethoxy-6,8,12,14,20,26-hexamethyl-23,27-epoxy-3*H*-pyrido[2,1-*c*][1,4]oxaazacyclohentriacontine-1,5,11,28,29(4*H*,6*H*,31*H*)-pentone CAS RN[®]: 159351-69-6.

DEFINITION

Everolimus contains NLT 95.0% and NMT 102.0% of everolimus ($C_{53}H_{83}NO_{14}$), calculated on the anhydrous and solvent-free basis. It may contain a suitable antioxidant.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

• PROCEDURE

Protect everolimus from exposure to oxygen. Protect solutions containing everolimus from light.

Solution A: 0.27 g/L of [monobasic potassium phosphate](#)

Solution B: [Acetonitrile](#)

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

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	60	40
5	43	57
23	36	64
31	0	100
36	0	100
37	60	40

Time (min)	Solution A (%)	Solution B (%)
45	60	40

System suitability solution: 0.5 mg/mL of [USP Everolimus System Suitability Mixture RS](#) in [acetonitrile](#)

Standard solution: 0.5 mg/mL of [USP Everolimus RS](#) in [acetonitrile](#)

Sample solution: 0.5 mg/mL of Everolimus in [acetonitrile](#)

Chromatographic system

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

Mode: LC

Detector: UV 275 nm

Column: 3-mm × 25-cm; 5-μm packing [L1](#)

Column temperature: 50°

Flow rate: 1.1 mL/min

Injection volume: 10 μL

System suitability

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

[NOTE—The relative retention times for 9-O-hydroxyethyl sirolimus, everolimus, and everolimus oxepane isomer are about 0.92, 1.0, and 1.1, respectively.]

Suitability requirements

Resolution: NLT 1.2 between 9-O-hydroxyethyl sirolimus and everolimus and NLT 1.5 between everolimus and everolimus oxepane isomer, *System suitability solution*

Relative standard deviation: NMT 2.0% for the sum of the everolimus and everolimus oxepane isomer peaks, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of everolimus ($C_{53}H_{83}NO_{14}$) in the portion of Everolimus taken:

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

r_U = sum of the peak responses of everolimus and everolimus oxepane isomer from the *Sample solution*

r_S = sum of the peak responses of everolimus and everolimus oxepane isomer from the *Standard solution*

C_S = concentration of [USP Everolimus RS](#) in the *Standard solution* (mg/mL)

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

F = percentage of sirolimus from the test for *Limit of Sirolimus*

Acceptance criteria: 95.0%–102.0% on the anhydrous and solvent-free basis

IMPURITIES

• **RESIDUE ON IGNITION (281):** NMT 0.1%

• **LIMIT OF ALCOHOL**

Analysis: See [Residual Solvents \(467\)](#).

Acceptance criteria: NMT 1.5%

• **ORGANIC IMPURITIES**

Protect everolimus from exposure to oxygen. Protect solutions containing everolimus from light and inject them within 2 h of preparation to minimize the effects of isomerization between everolimus and everolimus oxepane isomer.

Solution A, Solution B, and Mobile phase: Prepare as directed in the Assay.

System suitability solution: 5 mg/mL of [USP Everolimus System Suitability Mixture RS](#) in [acetonitrile](#). Use the solution within 24 h.

Sensitivity solution: 0.0025 mg/mL of [USP Everolimus RS](#) in [acetonitrile](#)

Standard solution: 0.05 mg/mL of [USP Everolimus RS](#) in [acetonitrile](#)

Sample solution: 5 mg/mL of Everolimus in [acetonitrile](#)

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 3-mm × 25-cm; 5-μm packing [L1](#)

Column temperature: 50°

Flow rate: 1.1 mL/min

Injection volume: 10 μL

System suitability