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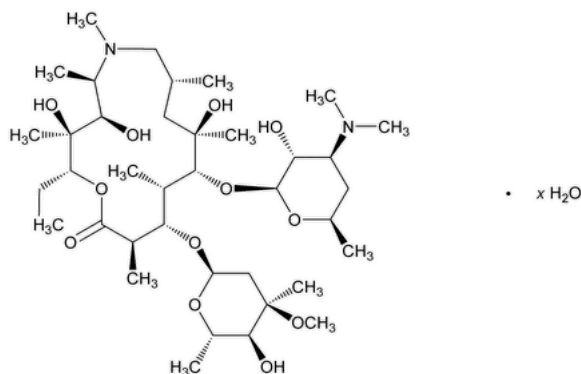
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Azithromycin


 $C_{38}H_{72}N_2O_{12}$ 749.00

 $C_{38}H_{72}N_2O_{12} \cdot H_2O$ 767.01

 $C_{38}H_{72}N_2O_{12} \cdot 2H_2O$ 785.03

1-Oxa-6-azacyclopentadecan-15-one, 13-[(2,6-dideoxy-3-C-methyl-3-O-methyl- α -L-ribo-hexopyranosyl)oxy]-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-11-[[3,4,6-trideoxy-3-(dimethylamino)- β -D-xylo-hexopyranosyl]oxy]-, [2R-(2R*,3S*,4R*,5R*,8R*,10R*,11R*,12S*,13S*,14R*)]; (2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)-13-[(2,6-Dideoxy-3-C-methyl-3-O-methyl- α -L-ribo-hexopyranosyl)oxy]-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-11-[[3,4,6-trideoxy-3-(dimethylamino)- β -D-xylo-hexopyranosyl]oxy]-1-oxa-6-azacyclopentadecan-15-one; 9-Deoxo-9a-aza-9a-methyl-9a-homoerythromycin A

Anhydrous CAS RN®: 83905-01-5.

Monohydrate CAS RN®: 121470-24-4.

Dihydrate CAS RN®: 117772-70-0.

DEFINITION

Azithromycin is anhydrous or contains 1 or 2 molecules of water of hydration. It contains the equivalent of NLT 945 µg/mg and NMT 1030 µg/mg of azithromycin ($C_{38}H_{72}N_2O_{12}$), calculated on the anhydrous basis.

IDENTIFICATION

- A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy: 197K:** If a difference appears in the IR spectra of the analyte and the Standard, dissolve equal portions of the test specimen and the USP Reference Standard in equal volumes of methanol. Evaporate the solutions to dryness on a water bath, and dry at 80° for 30 min under vacuum. Perform the test on the residues.
- B.** The retention time of the azithromycin peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

PROCEDURE

Solution A: 10 M potassium hydroxide**Solution B:** 6.7 g/L of dibasic potassium phosphate, adjusted with *Solution A* to a pH of 11.0**Solution C:** 6.7 g/L of dibasic potassium phosphate, adjusted with phosphoric acid to a pH of 8.0**Mobile phase:** Acetonitrile and *Solution B* (60:40)**Diluent:** Acetonitrile and *Solution C* (60:40)**System suitability solution:** 0.5 mg/mL each of USP Azithromycin RS and USP Azaerythromycin A RS prepared as follows. Dissolve USP Azithromycin RS and USP Azaerythromycin A RS first in acetonitrile, using 5% of the final volume, and then dilute with *Diluent* to volume.**Standard solution:** 0.53 mg/mL of USP Azithromycin RS prepared as follows. Dissolve USP Azithromycin RS first in acetonitrile, using 2% of the final volume, and then dilute with *Diluent* to volume.**Sample solution:** 0.53 mg/mL of Azithromycin prepared as follows. Dissolve Azithromycin first in acetonitrile, using 2% of the final volume, and then dilute with *Diluent* to volume.

Chromatographic system

(See [Chromatography \(621\), System Suitability.](#))**Mode:** LC

Detector: UV 210 nm**Column:** 4.6-mm × 25-cm; 5-µm packing [L67](#)**Column temperature:** 40°**Flow rate:** 1 mL/min**Injection volume:** 10 µL**System suitability****Samples:** *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for azaerythromycin A and azithromycin are 0.7 and 1.0, respectively.]

Suitability requirements**Resolution:** NLT 3.0 between azaerythromycin A and azithromycin, *System suitability solution***Tailing factor:** 0.8–1.5 for azithromycin, *Standard solution***Relative standard deviation:** NMT 1.10% for azithromycin, *Standard solution***Analysis****Samples:** *Standard solution* and *Sample solution*Calculate the quantity, in µg, of azithromycin (C₃₈H₇₂N₂O₁₂) in each milligram of Azithromycin taken:

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

 r_U = peak response from the *Sample solution* r_S = peak response from the *Standard solution* C_S = concentration of [USP Azithromycin RS](#) in the *Standard solution* C_U = concentration of Azithromycin in the *Sample solution* P = potency of [USP Azithromycin RS](#) (µg/mg of azithromycin)**Acceptance criteria:** 945–1030 µg/mg on the anhydrous basis**IMPURITIES**

- **RESIDUE ON IGNITION (281):** NMT 0.3%, moistening the charred residue with 2 mL of [nitric acid](#) and 5 drops of [sulfuric acid](#)

Change to read:• **ORGANIC IMPURITIES****Solution A:** 1.8 mg/mL of anhydrous [dibasic sodium phosphate](#) in [water](#). Adjust with [1 N sodium hydroxide](#) or [10% phosphoric acid](#) to a pH of 8.9.**Solution B:** [Acetonitrile](#) and [methanol](#) (3:1)**Solution C:** 1.73 mg/mL of [monobasic ammonium phosphate](#). Adjust with [ammonia TS](#) to a pH of 10.0 ± 0.05.**Solution D:** [Methanol](#), [acetonitrile](#), and *Solution C* (7:6:7)**Mobile phase:** See [Table 1](#).**Table 1**

Time (min)	Solution A (%)	Solution B (%)
0	50	50
25	45	55
30	40	60
80	25	75
81	50	50
93	50	50

System suitability solution: 0.0165 mg/mL of [USP Azithromycin Related Compound F RS](#) and 0.027 mg/mL of [USP Desosaminylazithromycin RS](#) in *Solution D***Standard solution:** 86 µg/mL of [USP Azithromycin RS](#) in *Solution D***Sample solution:** 8.6 mg/mL of Azithromycin in *Solution D***Chromatographic system**(See [Chromatography \(621\), System Suitability](#).)**Mode:** LC