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Vancomycin

$C_{66}H_{75}Cl_2N_9O_{24}$ 1449.25

Vancomycin

(*S*$_a$)-(3*S*,6*R*,7*R*,22*R*,23*S*,26*S*,36*R*,38a*R*)-44-[[2-*O*-(3-Amino-2,3,6-trideoxy-3-*C*-methyl-α-L-*lyxo*-hexopyranosyl)-β-D-glucopyranosyl]oxy]-3-(carbamoylmethyl)-10,19-dichloro-2,3,4,5,6,7,23,24,25,26,36,37,38,38a-tetradecahydro-7,22,28,30,32-pentahydroxy-6-[(2*R*)-4-methyl-2-(methylamino)valeramido]-2,5,24,38,39-pentaoxo-22*H*−8,11:18,21-dietheno-23,36-(iminomethano)-13,16:31,35-dimetheno-1*H*,16*H*-[1,6,9]oxadiazacyclohexadecino[4,5-*m*][10,2,16]-benzoxadiazacyclotetracosine-26-carboxylic acid;

[3*S*-[3*R**,6*S**(*S**),7*S**,22*S**,23*R**,26*R**,36*S**,38a*S**]]-3-(2-Amino-2-oxoethyl)-44-[[2-*O*-(3-amino-2,3,6-trideoxy-3-*C*-methyl-α-L-*lyxo*-hexopyranosyl)-β-D-glucopyranosyl]oxy]-10,19-dichloro-2,3,4,5,6,7,23,24,25,26,36,37,38,38a-tetra-decahydro-7,22,28,30,32-pentahydroxy-6-[[4-methyl-2-(methylamino)-1-oxopentyl]amino]-2,5,24,38,39-pentaoxo-22*H*−8,11:18,21-dietheno-23,36-(iminomethano)-13,16:31,35-dimetheno-1*H*, 16*H*-[1,6,9]oxadiazacyclohexadecino[4,5-*m*][10,2,16]-benzoxadiazacyclotetraine-26-carboxylic acid CAS RN®: 1404-90-6; UNII: 6Q205EH1VU.

DEFINITION

Vancomycin has a potency equivalent to NLT 950 µg/mg of $C_{66}H_{75}Cl_2N_9O_{24}$, calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

• **B.** Identification Tests—General, *Chloride*⟨191⟩**:** It does not meet the requirements of the test.

ASSAY

• Antibiotics—Microbial Assays ⟨81⟩

Sample solution: Transfer 100 mg of Vancomycin to a 100-mL volumetric flask. Add 50 mL of water and 1 mL of 0.1 N hydrochloric acid, and swirl to dissolve, using sonication if necessary. Dilute with water to volume. Dilute a volume of this solution with *Buffer B.4* to yield a *Test Dilution* having a concentration assumed to be equal to that of the median dose of the standard.

Analysis: Proceed as directed for Vancomycin in the chapter.

Acceptance criteria: NLT 950 µg/mg of vancomycin on the anhydrous basis

SPECIFIC TESTS

• Composition of Vancomycin

Buffer: Triethylamine and water (1:500). Adjust with phosphoric acid to a pH of 3.2.

Solution A: Acetonitrile, tetrahydrofuran, and *Buffer* (7:1:92)

Solution B: Acetonitrile, tetrahydrofuran, and *Buffer* (29:1:70)

Mobile phase: See *Table 1*. Make adjustments if necessary, changing the acetonitrile proportion in *Solution A* to obtain a retention time of 7.5–10.5 min for the main vancomycin peak.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
12	100	0
20	0	100

Time (min)	Solution A (%)	Solution B (%)
22	0	100
23	100	0
30	100	0

System suitability solution: 0.5 mg/mL of USP Vancomycin Hydrochloride RS in water. Heat at 65° for 48 h, and allow to cool.

Sample stock solution: Transfer 250 mg of Vancomycin to a 25-mL volumetric flask. Add 5 mL of *Solution A*, then add 0.1 N hydrochloric acid dropwise with swirling until dissolution is achieved. Dilute with *Solution A* to volume.

Sample solution: Dilute 2.0 mL of the *Sample stock solution* to 50 mL with *Solution A*.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 2 mL/min

Injection size: 20 µL

System suitability

Sample: *System suitability solution*

[NOTE—The elution order is compound 1, vancomycin B, and compound 2. Compound 2 elutes 3–6 min after the start of the period when the percentage of *Solution B* is increasing from 0% to 100%.]

Suitability requirements

Resolution: NLT 3.0 between compound 1 and vancomycin B

Column efficiency: NLT 1500 theoretical plates for the vancomycin B peak

Analysis

Samples: *Sample stock solution* and *Sample solution*

Where baseline separation is not achieved, peak areas are defined by vertical lines extended from the valleys between peaks to the baseline. The main component peak may include a fronting shoulder, which is attributed to monodechlorovancomycin. This shoulder should not be integrated separately.

Correct any peak observed in the chromatograms obtained from the *Sample stock solution* and *Sample solution* by subtracting the area response of any peak observed in the chromatogram of *Solution A* at the corresponding retention time.

Calculate the percentage of vancomycin B in the portion of Vancomycin taken:

$$\text{Result} = \{(D \times r_B)/[(D \times r_B) + r_A]\} \times 100$$

D = dilution factor, *Sample stock solution* to *Sample solution*, 25

r_B = corrected peak area response of the main peak from the *Sample solution*

r_A = sum of the corrected peak area responses of all the peaks, other than the main peak, from the *Sample stock solution*

Calculate the percentage of any individual peak, other than the main peak, in the portion of Vancomycin taken:

$$\text{Result} = \{r_i/[(D \times r_B) + r_A]\} \times 100$$

r_i = corrected peak area response of any individual peak, other than the main peak, from the *Sample stock solution*

D = dilution factor, *Sample stock solution* to *Sample solution*, 25

r_B = corrected peak area response of the main peak from the *Sample solution*

r_A = sum of the corrected peak area responses of all the peaks, other than the main peak, from the *Sample stock solution*

Acceptance criteria: NLT 92% of vancomycin B; NMT 3% of any individual peak other than the main peak

- **WATER DETERMINATION, *Method I*⟨921⟩:** NMT 20%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers.
- **USP Reference Standards** ⟨11⟩
  USP Vancomycin Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
VANCOMYCIN	Ying Han Associate Science & Standards Liaison	BIO42020 Biologics Monographs 4 - Antibiotics
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	BIO42020 Biologics Monographs 4 - Antibiotics

Chromatographic Database Information: Chromatographic Database

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