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Vancomycin Hydrochloride for Injection

DEFINITION

Vancomycin Hydrochloride for Injection is a sterile dry mixture of Vancomycin Hydrochloride and may contain a suitable stabilizing agent. It contains NLT 90.0% and NMT 115.0% of the labeled amount of vancomycin.

IDENTIFICATION

Change to read:

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

ASSAY

• **Antibiotics—Microbial Assays ⟨81⟩**

Sample solution 1 (where it is represented as being in a single-dose container)**:** Constitute a container of Vancomycin Hydrochloride for Injection in water corresponding to the volume of diluent specified in the labeling. Withdraw all of the withdrawable contents, using a suitable hypodermic needle and syringe. Dilute to an equivalent of 1 mg/mL of vancomycin with water.

Sample solution 2 (where it is packaged for dispensing)**:** Dissolve the contents of 1 container of Vancomycin Hydrochloride for Injection in water, and dilute with water to obtain a solution having a concentration of 1 mg/mL of vancomycin.

Sample solution 3 (where the label states the quantity of vancomycin in a given volume of constituted solution)**:** Constitute a container of Vancomycin Hydrochloride for Injection in water corresponding to the volume of diluent specified in the labeling. Dilute a portion to obtain a final concentration equivalent to 1 mg/mL of vancomycin in water.

Analysis: Proceed as directed in *Antibiotics—Microbial Assays* ⟨81⟩. [Note—Use a measured volume of the appropriate *Sample solution*, diluted quantitatively with *Buffer B.4* to yield a *Test Dilution* having a concentration assumed to be equal to the median dose level of the Standard.]

Acceptance criteria: 90.0%–115.0%

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩:** Meets the requirements

SPECIFIC TESTS

• **Particulate Matter in Injections ⟨788⟩:** Meets the requirements under small-volume injections

• **Bacterial Endotoxins Test ⟨85⟩:** NMT 0.33 USP Endotoxin Unit/mg of vancomycin

• **Sterility Tests ⟨71⟩:** It meets the requirements when tested as directed for *Test for Sterility of the Product to Be Examined, Membrane Filtration*, except to dissolve the specimen in water instead of in *Fluid A*.

• **pH ⟨791⟩:** 2.5–4.5, 50 mg/mL in water

• **Water Determination, *Method I*⟨921⟩:** NMT 5.0%

• **Injections and Implanted Drug Products ⟨1⟩, *Specific Tests, Completeness and clarity of solutions*:** Meets the requirements at the time of use.

• **Content of Vancomycin**

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

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

Solution C: Acetonitrile, tetrahydrofuran, and *Solution A* (29:1:70)

Mobile phase: See the gradient table below.

[Note—Make adjustments if necessary, changing the acetonitrile proportion in *Solution B* to obtain a retention time of 7.5–10.5 min for the main vancomycin peak.]

Time (min)	Solution B (%)	Solution C (%)
0	100	0

Time (min)	Solution B (%)	Solution C (%)
12	100	0
20	0	100
22	0	100
23	100	0
30	100	0

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

Sample solution 1: Equivalent to 10 mg/mL of vancomycin from Vancomycin Hydrochloride for Injection in *Solution B*

Sample solution 2: 0.4 mg/mL of vancomycin from *Sample solution 1* in *Solution B*

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 C* increases from 0% to 100%.]

Suitability requirements

Resolution: NLT 3.0 between compound 1 and vancomycin B

Column efficiency: NLT 1500 theoretical plates, calculated from the vancomycin B peak

Analysis

Samples: *Sample solution 1* and *Sample solution 2*

[Note—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.]

[Note—Correct any peak observed in the chromatograms obtained from *Sample solution 1* and *Sample solution 2* by subtracting the area response of any peak observed in the chromatogram of *Solution B* at the corresponding elution time.]

Measure the area responses for all of the peaks.

Calculate the percentage of vancomycin B in the specimen tested:

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

D = dilution factor, *Sample solution 1* to *Sample solution 2*, 25

r_B = corrected area response of the main peak from *Sample solution 2*

r_A = sum of the corrected area responses of all the peaks, other than the main peak, from *Sample solution 1*

Calculate the percentage of each other peak taken:

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

r_I = corrected area response of any individual peak, other than the main peak, from *Sample solution 1*

D = dilution factor, *Sample solution 1* to *Sample solution 2*, 25

Acceptance criteria: NLT 80.0% of vancomycin B; NMT 9.0% of any peak other than the main peak

- **Other Requirements:** It meets the requirements under *Injections and Implanted Drug Products ⟨1⟩*.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve as described in *Packaging and Storage Requirements ⟨659⟩, Injection Packaging, Packaging for constitution*.
- **Labeling:** Meets the requirements under *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*
- **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 HYDROCHLORIDE FOR INJECTION	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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