

# Vancomycin Injection

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click [www.uspnf.com/rb-vancomycin-inj-20220429](http://www.uspnf.com/rb-vancomycin-inj-20220429).

Change to read:

DEFINITION

Vancomycin Injection is a sterile solution of ▲Vancomycin or ▲ (RB 1-May-2022) Vancomycin Hydrochloride in Water for Injection. It contains NLT 90.0% and NMT 115.0% of the labeled amount of vancomycin ( $C_{66}H_{75}Cl_2N_9O_{24}$ ). It contains one or more suitable excipients.

IDENTIFICATION

• **A.** The retention time of the main vancomycin peak of the *Sample stock solution*, obtained as directed in *Composition of Vancomycin*, corresponds to that of a similarly prepared solution of [USP Vancomycin Hydrochloride RS](#).

ASSAY

• [ANTIBIOTICS—MICROBIAL ASSAYS \(81\)](#).

**Sample solution:** Allow a container of Injection to thaw, if applicable, and mix the solution. Dilute a portion 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:** 90.0%–115.0%

SPECIFIC TESTS

Change to read:

• **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            |
| 22         | 0              | 100            |
| 23         | 100            | 0              |
| 30         | 100            | 0              |

**System suitability solution:** Allow a container of Injection to thaw, if applicable, and mix the solution. Dilute a portion of the injection with [water](#) to obtain a solution containing 0.5 mg/mL of vancomycin. Heat at 65° for 24 h, and allow to cool.

**Sample stock solution:** Allow a container of Injection to thaw, if applicable, and mix the solution.

**Sample solution:** Equivalent to 0.4 mg/mL of ▲vancomycin or ▲ (RB 1-May-2022) vancomycin hydrochloride from the *Sample stock solution* in *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*

#### Suitability requirements

[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%.]

**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 from *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 Injection taken:

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

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

$r_B$  = 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 Injection 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*

$r_B$  = 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 88% of vancomycin B; NMT 4% of any individual peak other than the main peak

#### Change to read:

- **pH (791):** ▲ For products formulated with vancomycin hydrochloride, ▲ (RB 1-May-2022) 4.5–5.5 for products stored at room temperature; 3.0–5.0 for products maintained in a frozen state ▲; 3.9–4.3 for products formulated with vancomycin and stored at room temperature ▲ (RB 1-May-2022)
- **BACTERIAL ENDOTOXINS TEST (85):** NMT 0.33 USP Endotoxin Units/mg of vancomycin
- **PARTICULATE MATTER IN INJECTIONS (788):** Meets the requirements for small-volume injections or large-volume injections, whichever is applicable
- **STERILITY TESTS (71), [Test for Sterility of the Product to Be Examined](#), [Membrane Filtration](#):** Meets the requirements, except use [water](#) instead of diluting *Fluid A*
- **OTHER REQUIREMENTS:** Meets the requirements in [Injections and Implanted Drug Products \(1\)](#).