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Vancomycin for Infusion

General Notices

Action and use

Glycopeptide antibacterial.

DEFINITION

Vancomycin for Infusion is a sterile material consisting of Vancomycin Hydrochloride with or without excipients. It is supplied in a sealed container. It may be used to prepare a solution for oral administration.

If intended for administration as an Infusion, the contents of the sealed container comply with the requirements for Powders for Injections or Infusions stated under Parenteral Preparations and with the following requirements.

If intended for administration as an Oral Solution, the contents of the sealed container comply with the requirements for Powders and Granules for Oral Solutions and Oral Suspensions stated under Oral Liquids and with the following requirements.

IDENTIFICATION

A. In the test for Related substances and Vancomycin B, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 210 to 400 nm.

The UV spectrum of the principal peak in the chromatogram obtained with solution (1) is concordant with that of the peak in the chromatogram obtained with solution (2);

the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

B. Yield reaction A characteristic of *chlorides*, Appendix VI.

TESTS

Acidity

pH of a solution containing 5% w/v of Vancomycin Hydrochloride, 2.5 to 4.5, Appendix V L.

Clarity of solution

A solution containing 10.0% w/v of Vancomycin Hydrochloride is *clear*, Appendix IV A. The *absorbance* of the solution at 450 nm is not greater than 0.10, Appendix II B.

Related substances and vancomycin B

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions and the *normalisation* proceedure.

(1) Dissolve a quantity of the powder containing 0.1 g of Vancomycin Hydrochloride with 20 mL of *water* and dilute to 25 mL.
(2) 0.4% w/v of *vancomycin for system suitability EPCRS*.
(3) Expose 4 mg of *vancomycin for system suitability EPCRS* to 80-100% relative humidity at 42 ± 2° for at least 7 days. Allow to cool. Add 1 mL of *water* and dissolve the sample with the aid of ultrasound (generation of impurities B, D, E, G, and L).
(4) Dilute 1 volume of solution (2) to 100 volumes with 0.1% v/v of *acetic acid*. Dilute 1 volume of this solution to 10 volumes with the same solvent.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 2.1 mm) packed with *end-capped, charged-surface, ethylene-bridged, octadecylsilyl silica gel for chromatography (hybrid material)* (1.7 µm) (Acquity CSH C18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 0.3 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 280 nm.
(f) Use an autosampler temperature of 5°.
(g) Inject 2 µL of each solution.

MOBILE PHASE

Solution A 0.7% w/v solution of *tris(hydroxymethyl)aminomethane* previously adjusted to pH 8.1 with a 20% v/v solution of *glacial acetic acid*.

Mobile phase A 3 volumes of *acetonitrile*, 4 volumes of *methanol* and 93 volumes of solution A.

Mobile phase B 10 volumes of *acetonitrile*, 40 volumes of *methanol* and 50 volumes of solution A.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-7	88	12	isocratic
7-21	88→75	12→25	linear gradient
21-35	75→25	25→75	linear gradient
35-37	25	75	isocratic
37-38	25→88	75→12	linear gradient
38-45	88	12	re-equilibration

When the chromatograms are recorded under the prescribed conditions the retention times relative to vancomycin B (retention time, about 19 minutes) are: impurity E, about 0.4; impurity L, about 0.66; impurity B, about 0.70; impurity A, about 0.76; impurity F, about 0.82; impurity G, about 0.90; impurity H, about 0.94; impurity M, about 1.11; impurity I, about 1.14; impurity J, about 1.20; impurity D, about 1.24; impurity K, about 1.5 and impurity C, about 1.9.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3):

the *resolution* between the peaks due to impurity L and impurity B is between 1.5 to 5.0;

the *resolution* between the peaks due to impurity G and impurity H is between 1.5 to 4.0.

If the *resolution* between the peaks due to impurities L and B is greater than 5.0, adjust the pH of solution A to a lower value. If the *resolution* between the peaks due to impurities G and H is greater than 4.0, adjust the pH of solution A to a higher value.

LIMITS

Identify any peaks in the chromatogram obtained with solution (1) corresponding to vancomycin impurities A, C, F, H, I, J, K and M using the chromatogram obtained with solution (2) and any peaks corresponding to vancomycin impurities B, D, E, G, and L using the chromatogram obtained with solution (3).

In the chromatogram obtained with solution (1), integrate all peaks present with an area greater than the area of the principal peak in the chromatogram obtained with solution (4) to determine the total peak area. Calculate the percentage content of each of the components and impurities by *normalisation*:

the content of Vancomycin B is not less than 86.0%;

the area of any peak due to impurities A or H is not greater than 3.0%;

the sum of the areas of any peaks due to impurities B and E is not greater than 2.0%;

the area of any peak due to impurities D or J is not greater than 2.0%;

the area of any peak due to impurity C is not greater than 1.7%;

the area of any peak due to impurities F or M is not greater than 1.5%;

the area of any peak due to impurities G, I or K is not greater than 1.2%;

the area of any other *secondary peak* is not greater than 0.8%;

the sum of the areas of all the *secondary peaks* is not greater than 14.0%.

Water

Not more than 5.0% w/w, Appendix IX C. Use 0.5 g.

Bacterial endotoxins

Carry out the *test for bacterial endotoxins*, Appendix XIV C. Dissolve the contents of the sealed container in *tris-chloride buffer pH 7.4* prepared using *water BET* to give a solution containing 9000 IU of vancomycin per mL (solution A). The endotoxin limit concentration of solution A is 2.5 IU of endotoxin per mL.

ASSAY

Determine the weight of the contents of 10 containers as described in the test for *uniformity of weight*, Appendix XII C1, Powders for Parenteral Administration.

Mix the contents of the 10 containers and carry out the *microbiological assay of antibiotics*, Appendix XIV A. The precision of the assay is such that the fiducial limits of error are not less than 95% and not more than 105% of the estimated potency.

For a container of average content weight, the upper fiducial limit of error is not less than 95.0% and the lower fiducial limit of error is not more than 115.0% of the stated number of IU.

LABELLING

The label of the sealed container states (1) the total number of IU (Units) contained in it; (2) the number of IU (Units) per mg; (3) if it has been approved for oral administration.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Vancomycin Hydrochloride.