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Teicoplanin for Injection

Details for the public consultation of this monograph are as follows:

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Notes:	New Monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required.

Action and use

Glycopeptide antibacterial.

DEFINITION

Teicoplanin for Injection is a sterile material consisting of Teicoplanin with or without excipients. It is supplied in a sealed container.

The contents of the sealed container complies with the requirements stated for Powders for Injections or Infusions stated under [Parenteral Preparations](#) and with the following requirements.

IDENTIFICATION

The [infrared absorption spectrum, Appendix II A](#), of the powder for injection is concordant with the reference spectrum of teicoplanin (RS XXX).

TESTS

Composition

Carry out the method for [liquid chromatography, Appendix III D](#), using the following solutions and the *normalisation* procedure.

- Dissolve a quantity of the contents of a sealed container in sufficient [water](#) to produce a solution containing 200,000 IU of Teicoplanin per mL.
- 0.2% w/v [teicoplanin for identification EPCRS](#).
- Dilute 1 volume of solution (2) to 20 volumes.
- 0.002% w/v [mesityl oxide EPCRS](#) (impurity A).
- Dilute 1 volume of solution (1) to 100 volumes. Further dilute 1 volume of this solution to 10 volumes.

CHROMATOGRAPHIC CONDITIONS

- (a) Use a stainless steel column (25 cm × 4.6 mm) packed with [end-capped octadecylsilyl silica gel for chromatography](#) (5 µm) (Hypersil ODS-RP 18 is suitable).
- (b) Use gradient elution and the mobile phase described below.
- (c) Use a flow rate of 2.3 mL per minute.
- (d) Use an ambient column temperature.
- (e) Use a detection wavelength of 254 nm.
- (f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A 1 volume of [acetonitrile](#) and 9 volumes of a 0.3 % w/v solution of [sodium dihydrogen orthophosphate, anhydrous](#) previously adjusted to pH 6.0 with 1M [sodium hydroxide](#).

Mobile phase B 300 volumes of a 0.3 % w/v solution of [sodium dihydrogen orthophosphate, anhydrous](#) previously adjusted to pH 6.0 with 1M [sodium hydroxide](#) and 700 volume of [acetonitrile](#).

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-30	100→50	0→50	linear gradient
30-31	50→10	50→90	linear gradient
31-35	10	90	isocratic
35-36	10→100	90→0	linear gradient
36-40	100	0	re-equilibration

Use the chromatogram supplied with [teicoplanin for identification EPCRS](#) and the chromatogram obtained with solution (2) to identify the groups and components of teicoplanin.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to teicoplanin A₂₋₂ (retention time about 18 minutes) are detailed in the following table.

Group	Subgroup	Component	Relative retention
teicoplanin A ₃ group			≤0.70
		teicoplanin A ₃₋₁	about 0.43
teicoplanin A ₂ group			>0.70
	teicoplanin A ₂₋₁ group		>0.70 and <1.00
		teicoplanin A _{2-1a}	about 0.85
		teicoplanin A _{2-1b}	about 0.88
		teicoplanin A ₂₋₁	about 0.93

Group	Subgroup	Component	Relative retention
		teicoplanin A ₂₋₂	1.00
	teicoplanin A ₂₋₃ group		>1.00 and <1.12
		teicoplanin A ₂₋₃	about 1.03
		teicoplanin A ₂₋₄	about 1.12
	teicoplanin A ₂₋₅ group		>1.12 and <1.25
		teicoplanin A ₂₋₅	about 1.15
	teicoplanin A ₂₋₆ group		≥1.12
		teicoplanin-like related substance RS A _{2-6a}	about 1.25
		teicoplanin-like related substance RS A _{2-6b}	about 1.30
		teicoplanin-like related substance RS A _{2-6c}	about 1.38

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (2), the [resolution](#) between the peaks due to teicoplanin A₂₋₄ and teicoplanin A₂₋₅ is at least 1.0;

in the chromatogram obtained with solution (3), the [signal-to-noise ratio](#) of the peak due to teicoplanin A₂₋₂ is at least 40.

CALCULATION OF COMPONENTS

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 (5) and use the following equation to determine total peak area. Calculate the percentage content for each teicoplanin groups and components in the injection by *normalisation*.

$$S_2 + 0.83 \times S_3$$

where:

S_2 = sum of the areas of the peaks due to teicoplanin A₂ group;

S_3 = sum of the areas of the peaks due to teicoplanin A₃ group; disregard any peak due to impurity A;

LIMITS

The proportions are within the following limits:

- teicoplanin A₂ group, not less than 78%;
- teicoplanin A₃ group, not more than 17%.

Related substances

Carry out the method for [liquid chromatography, Appendix III D](#), as described in the test for Composition.

CALCULATION OF IMPURITIES

Use the chromatogram obtained with solution (2) to identify all peaks present above the disregard limit as teicoplanin-like related substances. Any peak present in any part of the chromatogram obtained with solution (1) that cannot be correlated to a peak above the disregard limit in solution (2) should be considered as a non-teicoplanin-like impurity, unless it is characterised by other means.

A teicoplanin-like related substance is defined as a substance that shares the same glycopeptide core structure of the parent molecule, composed of a linear heptapeptide aglycone, an α -D-mannose and an acetyl- β -D-glucosamine.

The R' side chains in the teicoplanin-like related substances RS A_{2-6a}, RS A_{2-6b} and RS A_{2-6c} are unknown.

Calculate the percentage content of the impurities in the injection by *normalisation*.

LIMITS

- any non-teicoplanin-like impurity: not more than 0.5%;
- total non-teicoplanin-like impurities: not more than 1.5%;
- Disregard any peak due to Impurity A.

Impurity A

Carry out the method for [liquid chromatography, Appendix III D](#), as described in the test for Composition.

CALCULATION OF IMPURITIES

Use the concentration of Impurity A in solution (3).

teicoplanin A_{2,2} retention time: about 18 minutes.

Relative retention: impurity A, about 0.6.

LIMITS

- impurity A: not more than 0.2%.

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 and (2) the number of IU (Units) per mg.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under [Teicoplanin](#).

DRAFT MONOGRAPH
SUBJECT TO CHANGE