ASSAY

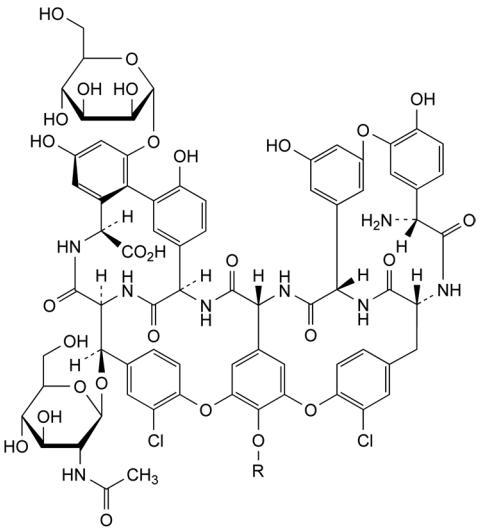
Dissolve 0.650 g in 25 mL of *water R*. Titrate with *1 M sodium hydroxide* using 0.5 mL of *phenolphthalein solution R* as indicator, until a pink colour is obtained.

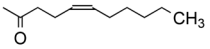
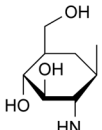
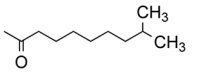
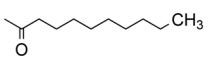
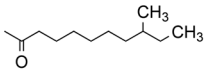
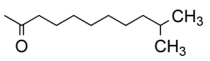
1 mL of *1 M sodium hydroxide* is equivalent to 75.05 mg of $C_4H_6O_6$.

01/2017:2358

TEICOPLANIN

Teicoplaninum



Teicoplanin	R	R'
A_{2-1} $C_{88}H_{95}Cl_2N_9O_{33}$ M. W.: 1878		
A_{2-2} $C_{88}H_{97}Cl_2N_9O_{33}$ M. W.: 1880		
A_{2-3} $C_{88}H_{97}Cl_2N_9O_{33}$ M. W.: 1880		
A_{2-4} $C_{89}H_{99}Cl_2N_9O_{33}$ M. W.: 1894		
A_{2-5} $C_{89}H_{99}Cl_2N_9O_{33}$ M. W.: 1894		
A_{3-1} $C_{72}H_{68}Cl_2N_8O_{28}$ M. W.: 1564	H	

DEFINITION

Mixture of glycopeptides produced by certain strains of *Actinoplanes teichomyceticus sp.*; the 6 principal components of the mixture are teicoplanin A_{2-1} to A_{2-5} and teicoplanin A_{3-1}.

Fermentation product.

Potency: minimum 900 IU/mg (anhydrous and sodium chloride-free substance).

CHARACTERS

Appearance: yellowish, amorphous powder.

Solubility: freely soluble in water, sparingly soluble in dimethylformamide, practically insoluble in ethanol (96 per cent *V/V*).

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *teicoplanin for identification CRS*.

B. Examine the chromatograms obtained in the test for composition and related substances.

Results: the principal peaks (teicoplanins A_{3-1}, A_{2-1}, A_{2-2}, A_{2-3}, A_{2-4} and A_{2-5}) in the chromatogram obtained with the test solution are similar in retention time and size to the principal peaks in the chromatogram obtained with reference solution (a).

TESTS

Appearance of solution. The solution is clear (*2.2.1*) and not more intensely coloured than reference solution BY_3 or B_4 (*2.2.2, Method I*).

Dissolve 0.8 g in 10 mL of *water R*.

pH (*2.2.3*): 6.5 to 7.5.

Dissolve 0.50 g in *carbon dioxide-free water R* and dilute to 10 mL with the same solvent.

Composition and related substances. Liquid chromatography (*2.2.29*): use the normalisation procedure.

Test solution. Dissolve 0.100 g of the substance to be examined in *water R* and dilute to 50.0 mL with the same solvent.

Reference solution (a). Dissolve 20 mg of *teicoplanin for identification CRS* in *water R* and dilute to 10.0 mL with the same solvent.

Reference solution (b). Dilute 1.0 mL of reference solution (a) to 10.0 mL with *water R*. Dilute 1.0 mL of this solution to 20.0 mL with *water R*.

Reference solution (c). Dissolve 50.0 mg of *mesityl oxide CRS* in *water R* and dilute to 25.0 mL with the same solvent. Dilute 1.0 mL of the solution to 10.0 mL with *water R*. Dilute 1.0 mL of this solution to 100.0 mL with *water R*.

Column:

- *size*: *l* = 0.25 m, Ø = 4.6 mm;
- *stationary phase*: spherical *end-capped octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase:

- *mobile phase A*: mix 900 mL of a 3.0 g/L solution of *anhydrous sodium dihydrogen phosphate R*, adjusted to pH 6.0 with *1 M sodium hydroxide*, and 100 mL of *acetonitrile R*;
- *mobile phase B*: mix 300 mL of a 3.0 g/L solution of *anhydrous sodium dihydrogen phosphate R*, adjusted to pH 6.0 with *1 M sodium hydroxide*, and 700 mL of *acetonitrile R*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 30	100 → 50	0 → 50
30 - 31	50 → 10	50 → 90
31 - 35	10	90

Flow rate: 2.3 mL/min.

Detection: spectrophotometer at 254 nm.

Injection: 20 µL.

Identification: use the chromatogram supplied with *teicoplanin for identification CRS* and the chromatogram obtained with reference solution (a) to identify the groups and impurities.

Relative retention of groups and impurities with reference to teicoplanin A_{2-2}:

- teicoplanin A_3 group ≤ 0.70;

Monographs T

- teicoplanin A_2 group > 0.70 and ≤ 1.25 and within this group:
  - teicoplanin $A_{2\text{-}2}$ = 1;
  - teicoplanin $A_{2\text{-}1}$ group < 1;
  - teicoplanin $A_{2\text{-}3}$ group > 1 and < 1.12;
  - teicoplanin $A_{2\text{-}4}$ = about 1.12;
  - teicoplanin $A_{2\text{-}5}$ group > 1.12 and ≤ 1.25;
- impurities > 1.25.

Relative retention of principal peaks of the groups with reference to teicoplanin $A_{2\text{-}2}$ (retention time = about 18 min): teicoplanin $A_{3\text{-}1}$ = about 0.43; teicoplanin $A_{2\text{-}1}$ = about 0.93; teicoplanin $A_{2\text{-}3}$ = about 1.04; teicoplanin $A_{2\text{-}4}$ = about 1.12; teicoplanin $A_{2\text{-}5}$ = about 1.14.

System suitability: reference solution (a):

- the chromatogram obtained is similar to the chromatogram supplied with *teicoplanin for identification CRS*;
- *resolution*: minimum 1.0 between the peaks due to teicoplanin $A_{2\text{-}4}$ and teicoplanin $A_{2\text{-}5}$.

Calculate the percentage content of the different components using the following equations:

$$\text{teicoplanin } A_2 \text{ group} = \frac{S_a}{S_a + 0.83 \times S_b + S_c} \times 100$$

$$\text{teicoplanin } A_{2\text{-}2} = \frac{S_2}{S_a + 0.83 \times S_b + S_c} \times 100$$

$$\text{teicoplanin } A_{2\text{-}1} \text{ group} = \frac{S_1}{S_a + 0.83 \times S_b + S_c} \times 100$$

$$\text{teicoplanin } A_{2\text{-}3} \text{ group} = \frac{S_3}{S_a + 0.83 \times S_b + S_c} \times 100$$

$$\text{teicoplanin } A_{2\text{-}4} = \frac{S_4}{S_a + 0.83 \times S_b + S_c} \times 100$$

$$\text{teicoplanin } A_{2\text{-}5} \text{ group} = \frac{S_5}{S_a + 0.83 \times S_b + S_c} \times 100$$

$$\text{teicoplanin } A_3 \text{ group} = \frac{0.83 \times S_b}{S_a + 0.83 \times S_b + S_c} \times 100$$

$$\text{impurities} = \frac{S_c}{S_a + 0.83 \times S_b + S_c} \times 100$$

S_a = sum of the areas of the peaks due to teicoplanin A_2 group in the chromatogram obtained with the test solution;

S_b = sum of the areas of the peaks due to teicoplanin A_3 group in the chromatogram obtained with the test solution; disregard any peak due to mesityl oxide;

S_c = sum of the areas of the peaks with a relative retention more than 1.25;

S_1 = sum of the areas of the peaks due to teicoplanin $A_{2\text{-}1}$ group in the chromatogram obtained with the test solution;

S_2 = area of the peak due to teicoplanin $A_{2\text{-}2}$ in the chromatogram obtained with the test solution;

S_3 = sum of the areas of the peaks due to teicoplanin $A_{2\text{-}3}$ group in the chromatogram obtained with the test solution;

S_4 = area of the peak due to teicoplanin $A_{2\text{-}4}$ in the chromatogram obtained with the test solution;

S_5 = sum of the areas of the peaks due to teicoplanin $A_{2\text{-}5}$ group in the chromatogram obtained with the test solution.

Limits:

- *teicoplanin A_2 group*: minimum 80.0 per cent;
- *teicoplanin $A_{2\text{-}2}$*: 35.0 per cent to 55.0 per cent;
- *teicoplanin $A_{2\text{-}1}$ group*: maximum 20.0 per cent;
- *teicoplanin $A_{2\text{-}3}$ group*: maximum 20.0 per cent;
- *teicoplanin $A_{2\text{-}4}$*: maximum 20.0 per cent;
- *teicoplanin $A_{2\text{-}5}$ group*: maximum 20.0 per cent;
- *teicoplanin A_3 group*: maximum 15.0 per cent;
- *total of impurities other than mesityl oxide with a relative retention more than 1.25*: maximum 5.0 per cent;
- *disregard limit*: the area of the peak due to teicoplanin $A_{2\text{-}2}$ in the chromatogram obtained with reference solution (b) (0.25 per cent).

Chlorides: maximum 5.0 per cent, expressed as sodium chloride (anhydrous substance).

Dissolve 1.000 g in 300 mL of *water R*, stir and acidify with 2 mL of *nitric acid R*. Titrate with *0.1 M silver nitrate*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M silver nitrate* is equivalent to 5.844 mg of NaCl.

Impurity A. Liquid chromatography (*2.2.29*) as described in the test for composition and related substances with the following modifications.

Injection: 20 µL of the test solution and reference solution (c).

Relative retention with reference to teicoplanin $A_{2\text{-}2}$ (retention time = about 18 min): impurity A = about 0.6.

Limits:

- *impurity A*: maximum twice the area of the principal peak in the chromatogram obtained with reference solution (c) (0.2 per cent).

Water (*2.5.12*): maximum 15.0 per cent, determined on 0.300 g.

Bacterial endotoxins (*2.6.14*): less than 0.31 IU/mg.

ASSAY

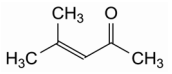
Carry out the microbiological assay of antibiotics (*2.7.2*), using the diffusion method. Use *teicoplanin CRS* as the reference substance.

STORAGE

Protected from light, at a temperature of 2 °C to 8 °C.

IMPURITIES

Specified impurities: A.

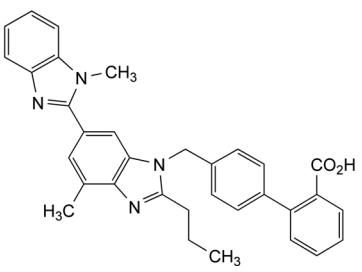


A. 4-methylpent-3-en-2-one (mesityl oxide).

07/2008:2154
corrected 6.3

TELMISARTAN

Telmisartanum



$C_{33}H_{30}N_4O_2$ M_r 514.6

[144701-48-4]