Edition: BP 2025 (Ph. Eur. 11.6 update)

Tigecycline for Infusion

General Notices

Action and use

Glycylcycline antibacterial.

DEFINITION

Tigecycline for Infusion is a sterile material consisting of *Tigecycline* with or without excipients. It is supplied in a sealed container.

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.

Content of tigecycline, $C_{29}H_{39}N_5O_8$

95.0 to 110.0% of the stated amount.

IDENTIFICATION

The *infrared absorption spectrum*, Appendix II A, is concordant with the reference spectrum produced with *tigecycline EPCRS*. If the spectra show differences, record a new spectrum after recrystallisation from *methanol*.

TESTS

Acidity

pH of a 1% w/v solution, 5.0 to 6.5. Appendix V L.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in a solution containing 0.44% w/v of *dipotassium hydrogen orthophosphate* and 0.05% w/v of *sodium hydrogensulfite* in *water*, adjusted to pH 8.0 with 1M *potassium hydroxide*. Store solutions at 10° and protect from light. Use solutions within 12 hours of preparation.
(1) Dissolve a quantity of the contents of the sealed container to produce a solution containing 0.05% w/v of Tigecycline.
(2) Dilute 1 volume of solution (1) to 100 volumes.
(3) Dilute 1 volume of solution (2) to 10 volumes.
(4) 0.05% w/v of *tigecycline for system suitability EPCRS* (impurity A), 0.00024% w/v of *tigecycline impurity B EPCRS* and 0.00024% w/v of *minocycline hydrochloride BPCRS* (impurity C).

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (3 µm) (Luna C18 is suitable).
(b) Use gradient elution and the mobile phase described below.

(c) Use a flow rate of 1.0 mL per minute.
(d) Use a column temperature of 30°.
(e) Use an autosampler temperature of 10°.
(f) Use a detection wavelength of 248 nm.
(g) Inject 25 µL of each solution.

MOBILE PHASE

Mobile phase A 50 volumes of *acetonitrile*, 950 volumes of a solution containing 0.46% w/v of *dipotassium hydrogen orthophosphate* and 0.10% w/v of *disodium edetate* in *water*, previously adjusted to pH 6.4 with *orthophosphoric acid*.
Mobile phase B 500 volumes of *acetonitrile*, 500 volumes of a solution containing 0.87% w/v of *dipotassium hydrogen orthophosphate* and 0.19% w/v of *disodium edetate* in *water*, previously adjusted to pH 6.4 with *orthophosphoric acid*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-2	85	15	isocratic
2-42	85→57	15→43	linear gradient
42-57	57→0	43→100	linear gradient
57-60	0	100	isocratic
60-61	0→85	100→15	linear gradient
61-68	85	15	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to tigecycline (retention time about 20 minutes) are: impurity 1, about 0.5; impurity B, about 0.6; impurity A, about 0.7; impurity 2, about 1.3; impurity C, about 1.6; impurity 3, about 1.7.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks due to impurity B and impurity A is at least 1.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity A is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (2%);

the area of any peak corresponding to impurity B is not greater than 0.7 times the area of the principal peak in the chromatogram obtained with solution (2) (0.7%);

the area of any peak corresponding to impurity C is not greater than twice the area of the principal peak in the chromatogram obtained with solution (3) (0.2%);

the area of any peak corresponding to impurity 2 is not greater than three times the area of the principal peak in the chromatogram obtained with solution (3) (0.3%);

the area of any peak corresponding to impurity 1 or impurity 3 is not greater than half the area of the principal peak in the chromatogram obtained with solution (2) (0.5% of each);

the area of any other *secondary peak* is not greater than twice the area of the principal peak in the chromatogram obtained with solution (3) (0.2%);

the sum of the areas of any *secondary peaks* is not greater than four times the area of the principal peak in the chromatogram obtained with solution (2) (4%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (3) (0.1%).

Water

Not more than 3.5%, Appendix IX C, Method III. Use the contents of one vial.

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.

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in a solution of 0.44% w/v of *dipotassium hydrogen orthophosphate* and 0.05% w/v of *sodium hydrogensulfite* in *water*, adjusted to pH 8.0 with 1M *potassium hydroxide*. Store solutions at 10° and protected from light.

(1) Dissolve a quantity of the mixed contents of 10 containers to produce a solution containing 0.01% w/v of Tigecycline.
(2) 0.01% w/v of *tigecycline EPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Prodigy ODS2 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use a column temperature of 30°.
(e) Use an autosampler temperature of 10°.
(f) Use a detection wavelength of 248 nm.
(g) Inject 20 µL of each solution.

MOBILE PHASE

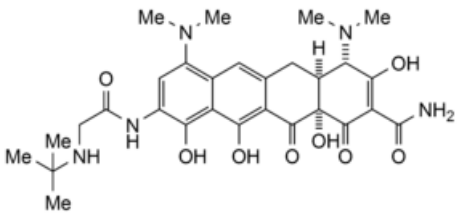
140 volumes of *acetonitrile* and 860 volumes of a solution of 0.44% w/v of *dipotassium hydrogen orthophosphate* and 0.093% w/v of *disodium edetate* in *water*, previously adjusted to pH 6.2 with *orthophosphoric acid*.

DETERMINATION OF CONTENT

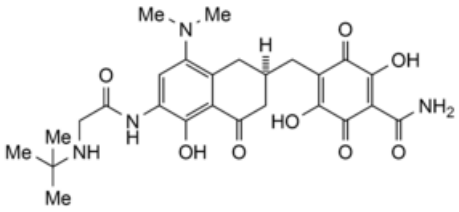
Calculate the content of tigecycline, $C_{29}H_{39}N_5O_8$ in a container of average content weight from the chromatograms obtained, using the declared content of $C_{29}H_{39}N_5O_8$ in *tigecycline EPCRS*.

IMPURITIES

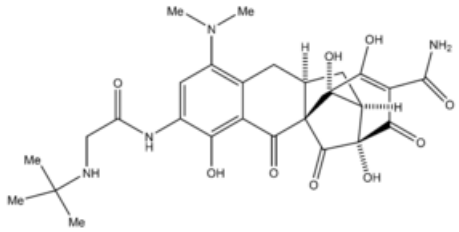
The impurities limited by the requirements of this monograph include those listed under Tigecycline and the following:



1. (4*S*,4a*S*,12a*S*)-9-[(*tert*-Butylamino)acetamido]-4,7-bis(dimethylamino)-3,10,11,12a-tetrahydroxy-1,12-dioxo-1,4,4a,5,12,12a-hexahydrotetracene-2-carboxamide



2. 4-{[(2*R*)-6-[(*tert*-Butylamino)acetamido]-8-(dimethylamino)-5-hydroxy-4-oxo-1,2,3,4-tetrahydronaphthalen-2-yl]methyl}-2,5-dihydroxy-3,6-dioxocyclohexa-1,4-diene-1-carboxamide



3. (1*S*,4a*R*,4b*R*,10a*R*,11a*S*)-7-[(*tert*-Butylamino)acetamido]-9-(dimethyamino)-1,4,4a,6-tetrahydroxy-2,5,12-trioxo-1,2,4a,5,10,10a,11,11a-octahydro-1,4b-methanobenzo[*b*]fluorene-3-carboxamide