Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-Dec-2020
Document Type: USP Monographs
DocId: GUID-453875BC-0BDC-4783-A5AB-924219CC1AF1_4_en-US
DOI: https://doi.org/10.31003/USPNF_M2073_04_01
DOI Ref: 5vk44

Tigecycline for Injection

DEFINITION

Tigecycline for Injection contains NLT 96.0% and NMT 116.0% of the labeled amount of tigecycline ($C_{29}H_{39}N_5O_8$). It may contain suitable stabilizers and buffers.

[NOTE—Handle standards and samples under moisture-controlled conditions to prevent degradation in quantitative applications where degradation could impact results.]

IDENTIFICATION

• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Dec-2020)

ASSAY

Change to read:

• **PROCEDURE**

Protect solutions containing tigecycline from light using low-actinic glassware. Store these solutions at 10° immediately after preparation and during analysis.

Buffer: 4.35 g/L of dibasic potassium phosphate and 0.93 g/L of edetate disodium; adjusted with phosphoric acid to a pH of 6.2

Mobile phase: Acetonitrile and *Buffer* (140:860)

Diluent: 4.35 g/L of dibasic potassium phosphate and 0.5 g/L of sodium bisulfite. Adjust with 1 N potassium hydroxide to a pH of 8.0

System suitability stock solution: Dissolve 10 mg of USP Tigecycline RS in 10.0 mL of water. Add 1 or 2 drops of trifluoroacetic acid, heat at about 65° for 15 min, and cool.

System suitability solution: Dilute 5.0 mL of the *System suitability stock solution* with water to 50.0 mL.

Standard solution: 0.1 mg/mL of USP Tigecycline RS in *Diluent*

Sample solution: Nominally 0.1 mg/mL of tigecycline from Tigecycline for Injection in *Diluent*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 248 nm. ▲For *Identification B*, use a diode array detector in the range of 190–400 nm.▲ (USP 1-Dec-2020)

Column: 4.6-mm × 15-cm; 5-µm packing L1

Temperatures

Autosampler: 10°

Column: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for the tigecycline epimer and tigecycline are about 0.67 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3.0 between the tigecycline epimer and tigecycline, *System suitability solution*

Tailing factor: 0.7–1.5, *Standard solution*

Relative standard deviation: NMT 1.1%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of tigecycline ($C_{29}H_{39}N_5O_8$) in the portion of Tigecycline for Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of tigecycline from the *Sample solution*

r_S = peak response of tigecycline from the *Standard solution*

C_S = concentration of USP Tigecycline RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of tigecycline in the *Sample solution* (mg/mL)

Acceptance criteria: 96.0%–116.0%

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩:** Meets the requirements

IMPURITIES

Change to read:

• **Organic Impurities**

Protect solutions containing tigecycline from light using low-actinic glassware. Store these solutions at 10° immediately after preparation and during analysis.

Solution A: Dissolve 4.35 g of dibasic potassium phosphate and 0.93 g of edetate disodium in 950 mL of water. Adjust with phosphoric acid to a pH of 6.4 ± 0.05, and add 50 mL of acetonitrile.

Solution B: Dissolve 4.35 g of dibasic potassium phosphate and 0.93 g of edetate disodium in 500 mL of water. Adjust with phosphoric acid to a pH of 6.4 ± 0.05, and add 500 mL of acetonitrile.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	85	15
40	57	43
55	0	100
58	0	100
59	85	15
66	85	15

Diluent: 4.35 g/L of dibasic potassium phosphate and 0.5 g/L of sodium bisulfite. Adjust with 1 N potassium hydroxide to a pH of 8.0

System suitability solution: 0.5 mg/mL of USP Tigecycline RS and 2.4 µg/mL of USP Tigecycline Related Compound B RS in *Diluent*

Sensitivity solution: 0.25 µg/mL of USP Tigecycline RS in *Diluent*

Standard solution: 0.005 mg/mL of USP Tigecycline RS in *Diluent*

Sample solution: Nominally 0.5 mg/mL of tigecycline in *Diluent* from the combined contents of NLT 5 vials ▲of Tigecycline for Injection▲ (USP 1-Dec-2020)

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 248 nm

Column: 4.6-mm × 15-cm; 3-µm packing L1

Temperatures

Autosampler: 10°

Column: 30°

Flow rate: 1 mL/min

Injection volume: 25 µL

System suitability

Samples: *System suitability solution*, *Sensitivity solution*, and *Standard solution*

Suitability requirements

Resolution: NLT 1.5 between tigecycline related compound B and the tigecycline epimer, *System suitability solution*

Tailing factor: 0.7–1.5, *Standard solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Tigecycline for Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of tigecycline from the *Standard solution*

C_S = concentration of USP Tigecycline RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of tigecycline in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Tigecycline open ring[a,b]	0.36	0.15
Tigecycline 12-oxo-11-hydroxy[c]	0.55	0.5
Tigecycline related compound B[d]	0.64	0.7
Tigecycline epimer[e]	0.74	2.0
Tigecycline	1.0	—
Tigecycline quinone analog[f]	1.3	0.3
Minocycline[g]	1.6	—
Tigecycline tricyclic analog[h]	1.7	0.5
Any individual unspecified degradation product	—	0.2
Total degradation products	—	6.0

[a] To be reported if there is a peak with maximum absorbance at either 390 or 640 nm. The impurity is quantitated at 248 nm. The system may resolve two peaks. The limit is for the sum of the two peaks.

[b] (3*S*,4*R*)-7-[2-(*tert*-Butylamino)acetamido]-3-[4-carbamoyl-2-(dimethylamino)-3,5,6-trihydroxybenzyl]-5-(dimethylimino)-1,4,8-trihydroxy-3,4,5,8-tetrahydronaphthalene-2-carboxylate.

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

[d] (4*S*,4a*S*,5a*R*,12a*S*)-9-Amino-4,7-bis(dimethylamino)-3,10,12,12a-tetrahydroxy-1,11-dioxo-1,4,4a,5,5a,6,11,12a-octahydrotetracene-2-carboxamide hydrochloride.

[e] (4*R*,4a*S*,5a*R*,12a*S*)-9-[2-(*tert*-Butylamino)acetamido]-4,7-bis(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-tetrahydroxy-1,11-dioxo-2-naphthacenecarboxamide.

[f] (*S*)-4-({6-[2-(*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-dienecarboxamide.

[g] Process impurities are controlled in the drug substance and are not to be reported here. They are not included in total impurities.

[h] (1*S*,4a*R*,4b*R*,10a*R*,11a*S*)-7-[2-(*tert*-Butylamino)acetamido]-9-(dimethylamino)-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.

SPECIFIC TESTS

• **pH** ⟨791⟩

Sample solution: Use the solution constituted as directed in the labeling.

Acceptance criteria: 4.5–5.5

• **Particulate Matter in Injections** ⟨788⟩

Sample solution: Use the solution constituted as directed in the labeling.

Acceptance criteria: Meets the requirements

Change to read:

• **Bacterial Endotoxins Test** ⟨85⟩**:** ▲Meets the requirements▲ (USP 1-Dec-2020)

• **Sterility Tests** ⟨71⟩**:** Meets the requirements

• **Other Requirements:** Meets the requirements in *Injections and Implanted Drug Products* ⟨1⟩

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve as described in *Packaging and Storage Requirements* ⟨659⟩*, Injection Packaging, Packaging for Constitution*. Store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Tigecycline RS

USP Tigecycline Related Compound B RS

(4*S*,4a*S*,5a*R*,12a*S*)-9-Amino-4,7-bis(dimethylamino)-3,10,12,12a-tetrahydroxy-1,11-dioxo-1,4,4a,5,5a,6,11,12a-octahydrotetracene-2-carboxamide hydrochloride.

$C_{23}H_{28}N_4O_7 \cdot HCl$ 508.95

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
TIGECYCLINE FOR INJECTION	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 45(5)

Current DocID: GUID-453875BC-0BDC-4783-A5AB-924219CC1AF1_4_en-US

DOI: https://doi.org/10.31003/USPNF_M2073_04_01

DOI ref: 5vk44