Post-reconstitution Stability of Telavancin with Commonly Used Diluents and Intravenous Infusion Solutions

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A B S T R A C T

Objective: The post-reconstitution chemical stability and microbial challenge hold time of nonpreserved telavancin for injection was determined using common reconstitution diluents and intravenous (IV) infusion solutions stored at room temperature with light (ambient) or at 2°C to 8°C without light (refrigeration).

Methods: Telavancin was reconstituted with 5% dextrose, 0.9% normal saline, or sterile water (15 mg/mL). Infusion solutions at 0.6 and 8.0 mg/mL were prepared in ViaFlex (polyvinyl chloride) IV bags (Baxter International Inc, Deerfield, Illinois) using 5% dextrose, 0.9% normal saline, or lactated Ringer's solution. Chemical stability was evaluated for up to 14 days under refrigeration and for up to 3 days under ambient conditions. Telavancin concentration and degradant levels were determined using a stability-indicating HPLC method. Solutions were subjected to microbial-challenge testing for up to 48 hours (ambient) or for up to 6 days (refrigeration).

Results: All reconstituted or infused telavancin solutions met the prespecified stability acceptance criteria after 2 days under ambient and minimum 7 days under refrigeration. Following inoculation with gram-positive and gram-negative microorganisms, telavancin infusion solutions stored under ambient conditions reduced or inhibited populations of all organisms up to 48 hours, except for *Serratia marcescens*, which exhibited growth of $> 0.5 \log_{10}$ after 12 hours. All refrigerated samples inhibited or reduced bacterial populations up to 6 days.

Conclusions: These results are supportive of a total hold time for reconstituted telavancin in vials plus the time in IV infusion solutions in polyvinyl chloride bags to not exceed 12 hours under ambient conditions and 7 days under refrigeration.

Introduction

The spread of methicillin-resistant *Staphylococcus aureus* (MRSA) as well as the emergence of strains with intermediate or full resistance to vancomycin has created an urgent need for novel antimicrobial agents with activity against resistant strains of *S. aureus.*

Telavancin for injection is a once-daily injectable lipoglycopeptide antibiotic with a dual mechanism of action that combines inhibition of cell wall synthesis and disruption of the functional integrity of the bacterial cell membrane.[1] It has shown bactericidal activity against clinically important gram-positive pathogens, including MRSA, streptococci, and VanB-type enterococci.[2,3] In

Phase 3 clinical trials, telavancin achieved its objective for non-inferiority to standard of care for treatment of complicated skin and skin structure infections (cSSSI) and hospital-acquired and ventilator-associated bacterial pneumonia caused by gram-positive pathogens.[4,5]

Telavancin is approved in the United States for the treatment of adults with cSSSI and hospital-acquired and ventilator-associated bacterial pneumonia (HAP/VAP) caused by susceptible isolates of *S aureus* when alternative treatments are not suitable. Telavancin is approved in Europe for the treatment of adults with nosocomial pneumonia, including VAP caused by MRSA and approved in Canada for the treatment of adults with cSSSI caused by susceptible gram-positive bacteria, including *S aureus* (both MRSA and methicillin-susceptible strains).

Telavancin for injection formulation contains hydroxypropyl-β-cyclodextrin and mannitol to enhance the solubility and stability. Telavancin for injection is provided as sterile, lyophilized powder

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within single-use 250 mg/vial and 750 mg/vial. The stability data of telavancin for injection intravenous (IV) solution in bags stored at −20°C were recently published[6]; however, there is no published information on the stability of telavancin for injection after reconstitution and dilution at refrigeration or room temperature with lights (ambient). These guidelines would be useful for infusion centers or hospital pharmacies where pharmacists routinely prepare large numbers of telavancin IV bags in advance so that they are readily available for patient use. This study examined the chemical stability and bacteriostatic/bactericidal properties of telavancin for injection after reconstitution and storage in polyvinyl chloride (PVC) bags of IV infusion solutions at concentrations simulating those used in clinical practice when stored under refrigerated conditions (2°C–8°C without light) and under ambient conditions (room temperature [20°C–25°C] with light) for up to 14 days.

Samples and Methods

Chemicals and reagents

Telavancin for injection 250-mg (lot 1283200) and 750-mg (lots 1229527, 1229529, and 1229530) vials (Ben Venue Laboratories, Inc, Bedford, Ohio) were used to prepare the samples. Sterile water for injection (SWFI) (Baxter International Inc, Deerfield, Illinois), 5% dextrose injection (D5W) (Baxter International Inc), 0.9% sodium chloride injection (normal saline [NS]) (Baxter International Inc), Lactated Ringer's solution (LR) (100 mL, 250 mL, or 500 mL) (Baxter International Inc), ViaFlex PVC IV bags (Baxter International Inc) and sterile syringes (30 cc and 60 cc) (Becton Dickinson, Franklin Lakes, New Jersey) were obtained commercially. Acetonitrile was high-performance liquid chromatography (HPLC)-grade or better (Burdick & Jackson, Muskegon, Michigan), and formic acid was American Chemical Society reagent grade (EMD, Gibbstown, New Jersey). All reagents were used without further purification. Purified water (analytical grade [resistivity of ≥ 18 MΩ.cm]) was generated in-house (MilliQ Advantage A10; EMD Millipore, Billerica, Massachusetts).

Sample preparation for chemical analysis

Samples of telavancin for injection were reconstituted in triplicate with appropriate amounts of the reconstitution diluents (D5W, SWFI, or NS) in the drug product vial with butyl rubber stoppers to yield a telavancin concentration of 15 mg/mL for both the 250 mg/vial and 750 mg/vial drug products. Vial reconstitution to 15 mg/mL is described in the telavancin for injection label.

Intravenous infusion solutions at target concentrations of 0.6 and 8 mg/mL—which cover the full range of concentrations to be used in clinical practice as specified on the label for telavancin for injection—were prepared in triplicate by transferring the required amount of reconstituted telavancin solutions to IV infusion bags of D5W, NS, or LR using sterile syringes. Samples reconstituted with D5W and NS were further diluted with D5W and NS, respectively, whereas samples reconstituted with SWFI were subsequently diluted with D5W, NS, or LR. The IV infusion bag target concentrations were calculated based on theoretical fill volumes of the IV bags; typical overfill volumes were not estimated.

Test conditions and drug attributes tested

Storage conditions tested were room temperature (20°C–25°C) with mixed standard laboratory fluorescent light and nondirect daylight from windows in the laboratory (ambient conditions), or at 2°C to 8°C without light (refrigerated conditions, uncovered). Stability assessments for the reconstituted solutions in vials were made at the outset for all sample solutions and at 0, 1, 3, and 7 days for the refrigerated conditions, and at 0, 1, and 2 days for the ambient conditions. For IV infusion solutions, the stability assessments were at 0, 3, 7, and 14 days for the refrigerated conditions and 0, 1, 2, and 3 days for the ambient conditions. The stability analysis for the 2-day samples stored under ambient conditions was only performed for samples that failed the acceptance criteria at 3 days. The selection of the stability study duration was based on the common practice at pharmacies and previous stability results of telavancin reconstituted solutions.

The drug attributes tested and the corresponding acceptance criteria were based on the US Food and Drug Administration-approved specification: visual appearance of dosage solution (conforms to USP < 1 >), telavancin concentration by HPLC (90.0%–110.0% of initial assay), level of degradant A by HPLC (≤ 1.0% wt/wt), level of degradant B (the primary degradation product of telavancin) by HPLC (≤ 3.0% wt/wt), and level of total degradation products by HPLC (≤ 4.0% wt/wt).

Telavancin concentration is expressed as milligrams per milliliter, whereas the degradant concentration is determined as the weight of each degradant/the weight of telavancin free base (salt form—telavancin hydrochloride) in the sample. Both of them are determined by comparing external telavancin reference standards injected during the HPLC analysis sequence. The response factors of degradants were determined to be similar to those of telavancin peak during the method validation, so the weight of each degradant/the weight of telavancin free base determination is based on the single reference standard of telavancin hydrochloride.

Physical attributes

The color and the clarity of the reconstituted and IV infusion solutions were determined by visual inspection of singular samples. Determinations of pH were performed using a Seven Easy pH meter (Mettler-Toledo International Inc, Columbus, Ohio).

HPLC analysis

A validated HPLC stability-indicating method analyzed telavancin and its impurity/degradants. The HPLC instrumentation (1100 series HPLC; Agilent Technologies, Santa Clara, California, and 2695/2996 HPLC; Waters Corporation, Milford, Massachusetts) included a C_{18} column (SunFire HPLC column 3.5 μm, C_{18}, 150 × 4.6 mm; Waters Corporation), maintained at 30°C, a vacuum degasser, an autosampler capable of maintaining temperatures at 5°C, a solvent delivery system, a column oven compartment, a diode-array detector, and Empower software (Empower Chromatography Data System; Waters Corporation). The mobile phase solutions consisted of acetonitrile:water:formic acid (2:98:0.05 vol/vol/vol) as mobile Phase A and acetonitrile:water:formic acid (60:40:0.05 vol/vol/vol) as mobile Phase B at a flow rate of 1 mL/min. The mobile phase A of the HPLC gradient was set as follows: 0 minutes = 90%, 20 minutes = 85%, 30 minutes = 80%, 50 minutes = 60%, and 50.5 minutes = 0% followed by 5 minutes washout and equilibrating period. The injection volume of 80 μL was used for all injections of standards and samples. Quantitation was performed by integration of the peaks at a detection wavelength of 230 nm for telavancin and its degradant peaks.

System suitability consisted of a relative standard deviation of ≤ 1.0% of telavancin peak area from 6 consecutive replicate injections (80 μL) of a system suitability solution, with tailing factor of ≤ 3, theoretical plates of ≥ 10,000, and resolution between peak I and peak II of ≥ 0.5, along with the relative standard deviation of ≤ 1% of telavancin peak area from

Table I
Results of pH test for reconstituted solutions in vials.

Vial strength (mg/vial)	Reconstituted solution	Refrigerated[*]				Ambient conditions[†]		
		Initial	1 d	3 d	7 d	Initial	1 d	2 d
250	SWFI	4.60	4.55	4.58	4.63	4.55	4.55	4.55
	D5W	4.51	4.51	4.46	4.55	4.47	4.46	4.51
	NS	4.66	4.65	4.63	4.58	4.67	4.65	4.63
750	SWFI	4.63	4.64	4.49	4.64	4.61	4.61	4.61
	D5W	4.65	4.63	4.57	4.68	4.74	4.65	4.69
	NS	4.69	4.71	4.60	4.78	4.71	4.70	4.78

D5W = 5% dextrose injection; NS = 0.9% sodium chloride injection (normal saline); SWFI = sterile water for injection.

[*] Stored at 2°C to 8°C without light.

[†] Room temperature with light.

3 reference standard solution injections bracketing the whole injection sequence.[6]

The HPLC method was validated in accordance with the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use Q2 (R1).[7] The detailed method validation information along with representative chromatograms that show retention times of degradant A and B were also published.[6]

Microbial challenge studies

Microbial challenge studies were performed by BioScreen Testing Service, Inc (Torrance, California), according to a study protocol approved by Theravance. Microbial cultures were prepared for inoculation with 10^3 to 10^4 CFU/mL *Pseudomonas aeruginosa* (ATCC 9027), *Escherichia coli* (ATCC 8739), *Serratia marcescens* (ATCC 14041), *Staphylococcus aureus* (ATCC 6538), *Candida albicans* (ATCC 10231), *Aspergillus niger* (ATCC 1604), *Staphylococcus epidermidis* (ATCC 700566), and vancomycin-resistant *Enterococcus faecalis* (ATCC 51575).

Telavancin for injection 750-mg vials were reconstituted to 15 mg/mL with D5W, NS, or SWFI, respectively. Telavancin for injection 250-mg vials were reconstituted to 15 mg/mL with D5W, NS, or SWFI, respectively, and further diluted in IV bags with D5W, NS, or LR to a target final telavancin concentration of 0.6 mg/mL. All sample preparations for microbial challenge studies were carried out in a Class 100 Laminar Flow Hood.

Reconstituted vial solutions and IV bag solutions were each inoculated with organisms representing a worst-case challenge of 10^3 to 10^4 CFU/mL. Solutions were tested for up to 48 hours under ambient conditions and 144 hours (6 days) under refrigerated conditions. Samples stored under ambient conditions were collected at time intervals of 0, 6, 8, 12, 24, and 48 hours. Samples stored at refrigerated conditions were collected and tested at time intervals of 0, 6, 8, 12, 24, 48, 72, and 144 hours. The specified acceptance criterion was no increase in microbial growth > 0.5 log from the time zero count.

Results

Chemical and physical stability of telavancin after reconstitution in a vial

Following reconstitution of each vial, the solution appearance was clear and essentially free of particulate matter.

The pH values of the reconstituted drug product solutions—regardless of the dosage strength, reconstitution solution, time point, or storage condition—was within the normal variation between 4.46 and 4.78 (**Table I**).

All reconstituted drug product combinations met the prespecified acceptance criteria with respect to the concentration of telavancin (**Table II**), degradant B (**Table III**), degradant A, and total degradants (degradant A + degradant B). The levels of degradant A and total degradants are not tabulated in detail, because there are no significant changes in the levels of degradant A, and all were < 0.2% wt/wt (compared with acceptance criterion of ≤ 1.0% wt/wt) throughout the study in either condition for reconstituted solutions ("significant change" for a drug product is defined by International Conference on Harmonisation as a 5% change in concentration from its initial values, or failure to meet the acceptance criteria for potency, degradation products, appearance, physical attributes, pH, and functionality test). Data on degradant B show that this primary degradant increases with time at both conditions; however, it remains within the acceptance criteria for at least 2 days under ambient conditions and for 7 days under refrigerated conditions, regardless of the type of reconstitution solution. The changes in the concentration are primarily caused by analytical variability and the increase of degradant B; nevertheless, the values remain within the product specification acceptance criteria for the durations and conditions tested.

Chemical/physical stability of telavancin with infusion solutions

The appearance for all infusion solutions was clear and essentially free of particulate matter at all time points. The pH values of

Table II
Percent of initial telavancin concentration in the reconstituted solution in vials at different time points.

Vial strength (mg/vial)	Reconstituted solution	Percent of initial assay mean values[*]						
		Refrigerated[†]				Ambient conditions[‡]		
		Actual initial concentration (FBE in mg/mL)	1 d	3 d	7 d	Actual initial concentration (FBE in mg/mL)	1 d	2 d
250	SWFI	15.17 (0.03)	100.1 (0.6)	100.7 (0.2)	100.7 (0.5)	15.21 (0.13)	99.6 (0.7)	98.8 (0.3)
	D5W	15.23 (0.05)	100.1 (0.1)	100.7 (0.6)	100.7 (0.4)	15.22 (0.09)	100.2 (0.9)	99.6 (0.7)
	NS	15.26 (0.05)	100.3 (0.1)	100.6 (0.3)	101.1 (0.1)	15.22 (0.15)	99.2 (0.1)	99.2 (0.2)
750	SWFI	15.23 (0.06)	101.5 (0.6)	101.5 (0.6)	100.8 (0.1)	15.26 (0.03)	100.9 (0.1)	100.0 (0.2)
	D5W	14.92 (0.12)	101.4 (0.6)	101.8 (0.6)	101.0 (0.6)	14.96 (0.03)	100.7 (0.5)	99.9 (0.2)
	NS	15.09 (0.08)	100.8 (0.1)	100.7 (0.2)	100.1 (0.3)	15.07 (0.08)	100.2 (0.5)	99.7 (0.6)

D5W = 5% dextrose injection; FBE = free base equivalent; NS = 0.9% sodium chloride injection (normal saline); SWFI = sterile water for injection.

[*] Values are presented as mean (SD) of triplicate determination.

[†] Stored at 2°C to 8°C without light.

[‡] Room temperature with light.

Table III
Degradant B (% wt/wt) results of reconstituted solution in vials at different time points.

Vial strength (mg/vial)	Reconstituted solution	Refrigerated[*]				Ambient conditions[†]		
		Initial	1 d	3 d	7 d	Initial	1 d	2 d
250	SWFI	1.06	1.17	1.30	1.55	1.04	1.60	2.10
	D5W	1.06	1.16	1.27	1.50	1.05	1.55	2.04
	NS	1.12	1.15	1.24	1.38	1.12	1.48	1.86
750	SWFI	1.02	1.19	1.22	1.47	1.00	1.57	2.10
	D5W	1.02	1.16	1.20	1.47	0.99	1.56	2.07
	NS	1.06	1.18	1.17	1.43	1.08	1.53	1.95

D5W = 5% dextrose injection; NS = 0.9% sodium chloride injection (normal saline); SWFI = sterile water for injection.

[*] Stored at 2°C to 8°C without light.

[†] Room temperature with light.

the drug product infusion solutions from various combinations of reconstitution solutions and IV solutions at different time points or storage conditions are shown in **Table IV**. No significant changes over time were observed for all tested infusion solutions.

The concentrations of telavancin in IV infusion solutions held in commercially available PVC IV bags at different time points are shown in **Table V**. The telavancin concentrations of IV infusion solution meet the prespecified specification at all time points. Due to the typical overfill (5%–15% in volume) of infusion solution bags, the actual initial concentrations of reconstituted solutions are 5% to 15% lower than the theoretical concentration.

The levels of degradant B in IV infusion solutions held in commercially available PVC IV bags with different combinations of reconstitution solutions and IV solutions are shown in **Table VI**. The levels of degradant B for IV infusion solutions are within the acceptance criteria of ≤ 3.0% after 3 days under ambient conditions for all IV solutions, except when D5W is used as the IV dosing solution at 0.6 mg/mL. In this case, the levels of degradant B are within the acceptance criteria of ≤ 3.0% after 2 days under ambient conditions. The levels of degradant A and total degradants are not shown because there were no significant changes.

Microbial challenge hold time of telavancin in various solutions

Ambient conditions: Reconstituted solution in vials

Reconstituted telavancin for injection solutions were challenged with yeast; mold; and gram-positive and gram-negative microorganisms including *S. aureus, S. epidermidis,* vancomycin-resistant

E. faecalis, C. albicans, A. niger P aeruginosa, and *E. coli* to represent a worst-case condition in the event of an inadvertent contamination during the reconstitution or dilution of the product for infusion. The results showed fungicidal, bactericidal, or bacteriostatic properties (no growth or growth < 0.5 $\log_{10}$) when stored under ambient conditions for at least 48 hours, except for gram-negative organism *S. marcescens*. The solution challenged with *Serratia marcescens* showed a growth of 0.6 to 0.9 $\log_{10}$ at 48 hours in SWFI, NS, and D5W; whereas there is no growth or growth < 0.5 $\log_{10}$ at 0, 6, 8, 12, and 24 hours.

Ambient conditions: Solution in IV bags

Telavancin for injection reconstituted with D5W, NS, or SWFI solutions that were further diluted in IV bags containing D5W, NS, or LR were also challenged with the same microorganisms. The results exhibited bactericidal or bacteriostatic properties for D5W and NS IV bags stored under ambient conditions for at least 48 hours, except for *S. marcescens*, which showed a growth of 0.5 to 1.2 $\log_{10}$ at 24 and 48 hours, respectively; there was no growth or growth < 0.5 $\log_{10}$ at 0, 6, 8, and 12 hours. Telavancin for injection, reconstituted with SWFI and diluted in a LR IV bag solution, showed that all microorganisms grew > 0.5 $\log_{10}$ at 24 and 48 hours but not at 0, 6, 8, and 12 hours.

Based on the microbial growth data of reconstituted vial solutions and IV bag solutions stored under ambient conditions, a maximum 12-hour hold period is justified.

Refrigerated conditions: Reconstituted solution in vials and solution in IV bags

Test results for all refrigerated samples showed either stasis or significant logarithmic reductions in microbial populations over the 144-hour (6-day) hold time. Based on the flat or negative slopes of the microbial populations over the challenge period, a maximum 7-day hold period is justified.

Discussion

The physical and chemical stability and microbial hold time of telavancin for injection in therapeutic reconstituted solutions and IV infusion solutions in PVC bags under conditions that reflect typical hospital practices were evaluated in this study. The IV infusion solutions tested in this study are those specified in the label of telavancin for injection. These data establish a reference for proper storage and handling of this drug product upon reconstitution and dilution into PVC IV bags.

Table IV
Results of pH testing for intravenous infusion solutions in polyvinyl chloride bags at different time points.

Reconstituted solution	Dosing solution	Dose strength (mg/mL)	Refrigerated[*]				Ambient conditions[†]			
			Initial	3 d	7 d	14 d	Initial	1 d	2 d	3 d
SWFI	LR	0.6	5.53	5.46	5.43	5.84	5.81	5.88	NT	5.68
SWFI	D5W	0.6	5.33	4.73	4.92	5.09	5.20	4.83	5.03	4.81
SWFI	NS	0.6	5.10	4.88	5.14	5.21	5.12	4.90	NT	4.88
D5W	D5W	0.6	5.43	4.82	5.18	5.07	5.12	5.11	5.14	4.83
NS	NS	0.6	5.00	4.96	5.00	5.10	4.86	4.79	NT	4.94
SWFI	LR	8	5.11	5.05	5.13	5.17	5.09	5.06	NT	5.03
SWFI	D5W	8	4.71	4.69	4.76	4.81	4.70	4.64	NT	4.64
SWFI	NS	8	4.67	4.75	4.81	4.90	4.73	4.64	NT	4.77
D5W	D5W	8	4.62	4.72	4.86	4.91	4.57	4.59	NT	4.71
NS	NS	8	4.60	4.78	4.80	4.94	4.63	4.60	NT	4.78

D5W = 5% dextrose injection; LR = Lactated Ringer's injection; NS = 0.9% sodium chloride injection (normal saline); NT = not tested; SWFI = sterile water for injection.

[*] Stored at 2°C to 8°C without light.

[†] Room temperature with light.

Table V
Percent of initial assay mean values[*] in intravenous infusion solution in polyvinyl chloride bags at different time points

Reconstituted solution	Dosing solution	Refrigerated[†]				Ambient conditions[‡]			
		Actual initial concentration[§] (mg/mL)	3 d	7 d	14 d	Actual initial concentration (mg/mL)	1 d	2 d	3 d
SWFI	LR	0.57 (0.00)	97.1 (1.1)	98.6 (0.5)	98.7 (0.8)	0.57 (0.00)	98.9 (1.1)	NT	96.6 (0.6)
SWFI	D5W	0.58 (0.01)	97.4 (0.9)	98.7 (1.3)	99.3 (1.3)	0.59 (0.02)	98.5 (2.5)	97.5 (3.1)	94.6 (3.9)
SWFI	NS	0.58 (0.00)	95.4 (1.4)	97.8 (1.3)	99.0 (0.7)	0.59 (0.01)	98.3 (1.4)	NT	94.6 (2.2)
D5W	D5W	0.56 (0.01)	97.5 (1.0)	99.1 (2.0)	98.3 (1.2)	0.55 (0.00)	99.1 (0.6)	97.9 (0.5)	96.4 (0.2)
NS	NS	0.57 (0.01)	95.4 (0.8)	98.6 (1.4)	99.0 (0.7)	0.58 (0.01)	99.7 (1.2)	NT	95.8 (1.0)
SWFI	LR	7.59 (0.05)	100.3 (0.7)	100.1 (0.5)	100.0 (0.7)	7.41 (0.05)	100.6 (0.8)	NT	98.5 (1.1)
SWFI	D5W	7.74 (0.08)	99.1 (0.9)	100.4 (1.0)	99.1 (1.2)	7.12 (0.13)	100.0 (1.4)	NT	99.0 (1.8)
SWFI	NS	7.53 (0.08)	101.1 (1.0)	100.9 (1.3)	100.4 (1.1)	7.64 (0.05)	99.9 (0.8)	NT	98.9 (0.9)
D5W	D5W	7.37 (0.07)	101.1 (0.9)	100.7 (0.6)	100.1 (1.1)	7.45 (0.04)	99.9 (0.5)	NT	98.7 (0.9)
NS	NS	7.23 (0.02)	101.9 (0.8)	101.4 (0.8)	100.5 (0.8)	7.50 (0.03)	98.9 (0.8)	NT	97.5 (0.3)

D5W = 5% dextrose injection; LR = Lactated Ringer's injection; NS = 0.9% sodium chloride injection (normal saline); NT = not tested; SWFI = sterile water for injection.

[*] Values are presented as mean (SD) of triplicate determination.
[†] Stored at 2°C to 8°C without light.
[‡] Room temperature with light.
[§] Due to the typical overfill (5%–15% in volume) of infusion solution bags, the actual initial concentrations of reconstituted solutions are 5% to 15% lower than the theoretical concentration.

As with all sterile products for injection, particularly because no preservative is present in telavancin for injection, aseptic technique must be strictly observed when preparing product for administration.

Conclusions

The chemical and physical stability and microbial challenge data reported here support a postconstitution hold time of 12 hours under ambient conditions and 7 days under refrigerated conditions for both reconstituted telavancin for injection in a vial and IV infusion solutions in a PVC IV bag when prepared with the diluents tested in this study. The total time in the vial, plus the time in the infusion bag, should not exceed 12 hours at room temperature and 7 days under refrigeration at 2°C to 8°C.

Acknowledgments

Conflicts of Interest

Table VI
Degradant B (% wt/wt) of intravenous dosing solution in polyvinyl chloride bags.

Reconstituted solution	Dosing solution	Dose strength (mg/mL)	Refrigerated[*]				Ambient conditions[†]			
			Initial	3 d	7 d	14 d	Initial	1 d	2 d	3 d
SWFI	LR	0.6	1.08	1.38	1.62	1.90	1.12	1.55	NT	2.32
SWFI	D5W	0.6	1.10	1.49	1.87	2.38	1.13	1.78	2.62[‡]	3.18[‡]
SWFI	NS	0.6	1.09	1.51	1.79	2.23	1.11	1.72	NT	2.98
D5W	D5W	0.6	1.08	1.52	1.86	2.43	1.08	1.83	2.64[‡]	3.20[‡]
NS	NS	0.6	1.13	1.56	1.80	2.27	1.16	1.77	NT	2.98
SWFI	LR	8	1.08	1.38	1.65	1.91	1.12	1.57	NT	2.60
SWFI	D5W	8	1.08	1.45	1.69	2.10	1.08	1.66	NT	2.80
SWFI	NS	8	1.10	1.40	1.61	1.97	1.12	1.57	NT	2.59
D5W	D5W	8	1.08	1.42	1.70	2.09	1.08	1.62	NT	2.82
NS	NS	8	1.14	1.40	1.62	1.88	1.13	1.57	NT	2.54

D5W = 5% dextrose injection; LR = Lactated Ringer's injection; NS = 0.9% sodium chloride injection (normal saline); NT = not tested; SWFI = sterile water for injection.

[*] Stored at 2°C to 8°C without light.
[†] Room temperature with light.
[‡] Outside of acceptance criteria defined in the protocol. Samples at 2-day time points were analyzed.

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