Telavancin (Vibativ), a New Option for the Treatment of Gram-Positive Infections

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INTRODUCTION

In recent years, the development of bacterial resistance has escalated, especially among gram-positive microorganisms. Pathogens identified as Staphylococcus species (spp.) and Enterococci spp. have become extremely challenging to eradicate, particularly vancomycin-resistant strains. Vancomycin (Vancocin, ViroPharma) has been the mainstay for treating gram-positive infections for decades; however, since the emergence of vancomycin-resistant organisms, which have become increasingly frequent in clinical practice, its use has ultimately been replaced by other antimicrobials: linezolid (Zyvox, Pfizer), daptomycin (Cubicin, Cubist), quinupristin/dalfopristin (Synercid, King), and tigecycline (Tygacil, Pfizer). As resistance continues to develop among newer agents, an innovative class of antimicrobials known as lipoglycopeptides has emerged. A novel entity, lipoglycopeptide, telavancin (Vibativ, Theravance/Astellas), has been the mainstay for treating gram-positive infections for decades; however, since the emergence of vancomycin-resistant organisms, which have become increasingly frequent in clinical practice, its use has ultimately been replaced by other antimicrobials: linezolid (Zyvox, Pfizer), daptomycin (Cubicin, Cubist), quinupristin/dalfopristin (Synercid, King), and tigecycline (Tygacil, Pfizer). As resistance continues to develop among the newer agents, an innovative class of antimicrobials known as lipoglycopeptides has emerged. A novel entity, lipoglycopeptide, telavancin (Vibativ, Theravance/Astellas), was granted FDA approval in September 2009 for the treatment of adults with complicated skin and skin structure infections (cSSSIs). Telavancin is currently recommended for patients with susceptible or highly suspected gram-positive bacterial infections. As more data become available, it is likely that telavancin will be found to have additional uses in the management of various infections.

CHEMICAL STRUCTURE

Figure 1A illustrates the chemical structure of telavancin HCl, which is synthetically derived from vancomycin. As a lipoglycopeptide, telavancin possesses a hydrophilic side chain, resulting in a prolonged half-life as well as a lipophilic tail attached to the heptapeptide core. Figure 1B illustrates the chemical structure of vancomycin as a comparison.

INDICATIONS AND USAGE

Telavancin is approved for the treatment of adults with cSSSIs caused by susceptible gram-positive microorganisms. The ATTAIN trials are being conducted in an effort to earn an additional FDA-approved indication for telavancin in the treatment of hospital-acquired pneumonia.

CLINICAL PHARMACOLOGY

Telavancin’s mechanism of action on susceptible bacteria exerts dual effects in eradicating pathogens. Initially, telavancin causes inhibition of bacterial cell wall synthesis by directly interfering with polymerization and cross-linkage of the peptidoglycan layer, followed by disruption of bacterial cell membranes via depolarization, leading to impaired barrier function. The spectrum of activity has been evident with numerous gram-positive microorganisms, including Staphylococcus, Streptococcus, Enterococcus spp. and anaerobic bacteria. A list of bacteria susceptible to the effects of telavancin is presented in Table 1.

Bacterial Resistance

Some strains of vancomycin-resistant enterococci (VRE) have been identified as having reduced susceptibility to telavancin, although cross-resistance between telavancin and other antimicrobials has not been established. One concern is the possibility of superinfection development during telavancin therapy. If a superinfection occurs or is suspected, vigilant monitoring and appropriate measures must be taken.

Disclosure: The authors report no commercial or industrial relationships in regard to this article.
and three strains of Enterococcus: E. faecalis, E. faecium, and vancomycin-resistant E. faecium

Telavancin’s excellent activity is based on the area-under-the-bacterial-kill-curve (AUB–KC) at 24 and 48 hours. Its early killing effect is greater than that of vancomycin and teicoplanin (Targocid, Sanofi-Aventis) (P < 0.05).

In healthy young adults, telavancin demonstrated linear pharmacokinetics following single doses of 5 to 12.5 mg/kg and multiple doses of 7.5 to 15 mg/kg, administered once daily for up to seven days. Pharmacokinetic properties were evaluated in several studies.

In a double-blind, placebo-controlled, randomized study conducted by Shaw et al., 54 healthy men received single and multiple doses of telavancin.3 With a dose of 10 mg/kg per day given over a period of 120 minutes, the maximum concentration (Cmax) was 87.5 mcg/mL, the AUC from time zero to infinity (AUC0–∞) was 7.5 mcg-hours/mL, and the half-life was 7.5 hours. Multiple doses of 7.5, 12.5, and 15 mg/kg, infused over a period of 30 minutes, were also evaluated over a seven-day period. No significant changes were reported in measured pharmacokinetics on day 1 compared with day 7. Steady-state concentrations at doses of 7.5, 12.5, and 15 mg/kg per day were 96.7 mcg/mL, 151 mcg/mL, and 203 mcg/mL, respectively. The AUC concentrations were 700, 1,033, and 1,165 mcg-hours/mL, respectively. The half-life was six to nine hours. Renal clearance was 10 to 15 mL/hours per kg.

A similar study, conducted by Wong et al., evaluated 79 men and women who received telavancin 7.5 mg/kg and 15 mg/kg over a period of 60 minutes.4 On day 3, the Cmax was 87.5 and 186 mg/L; the AUC0–24 hours was 785 mcg-hours/mL, and the mean half-life was 7.41 hours. Penetration of telavancin into the epithelial lining fluid was considerable after eight hours, with a mean Cmax of 3.73 mcg/L. Telavancin’s penetration of alveolar macrophages was significant, with a Cmax of 45 mcg/L after 12 hours.

In vitro studies concluded that telavancin did not establish any active metabolites.3 In addition, the major components of human cytochrome P450 (CYP 450) isoenzymes did not appear to be affected by telavancin’s metabolism. As a result, inhibitors or inducers of these isoenzymes should not influence the clearance of telavancin. Furthermore, the excretion of telavancin occurs primarily by the kidney. According to the manufacturer, a study enrolling healthy men using radiolabeled telavancin identified three hydroxylated metabolites; however, the exact mechanism of metabolism remains unknown.1

**Efficacy and Safety in Clinical Trials**

**Skin Infections**

Two randomized, double-blind, controlled trials, FAST and FAST 2, evaluated telavancin against standard antimicrobial therapy for use in cSSSIs. In FAST, patients with a creatinine clearance (CrCl) of less than 50 mL/minute continued on page 133
Cultured MRSA at baseline was noted in 48 patients. Of these patients, 82% of patients in the telavancin group and 69% of the standard-therapy patients achieved cures. Patients identified as microbiologically evaluable (n = 112) in both the telavancin group and standard therapy group (n = 42) patients (75%) were considered to have been cured of the baseline pathogen at the end-of-therapy evaluation ($P = 0.83$).

During the test-of-cure evaluations, pathogens were considered eradicated in 44 patients (80%) receiving telavancin and in 46 patients (82%) receiving standard therapy ($P = 0.83$). During the test-of-cure evaluation, eradication of MRSA was reported in 16 telavancin patients.

### The FAST Trial$^{11}$

Success rates of telavancin were similar to those of standard therapy, not only at the end-of-therapy evaluation but also at the test-of-cure visit. In the all-treated population (n = 167) and the clinically evaluable population (n = 141), both therapies resulted in cures in 66 patients at the test-of-cure evaluations (79% for telavancin, 80% for standard therapy; $P = 0.53$).

At the baseline evaluation, $S. aureus$ was isolated in the telavancin patients (n = 50) and in the standard therapy group (n = 52). Cure was achieved at the test-of-cure visit in 40 patients (80%) who received telavancin and in 40 patients (77%) who received standard therapy.

### Table 2: Study Population and Baseline Patient Characteristics in the FAST Trials

<table>
<thead>
<tr>
<th>Study Population</th>
<th>Telavancin (%)</th>
<th>Standard Treatment (%)</th>
<th>Telavancin (%)</th>
<th>Standard Treatment (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients randomized</td>
<td>84 (100)</td>
<td>85 (100)</td>
<td>103</td>
<td>98</td>
</tr>
<tr>
<td>All treated*</td>
<td>84 (100)</td>
<td>83 (98)</td>
<td>100 (97)</td>
<td>95 (97)</td>
</tr>
<tr>
<td>Clinically evaluable†</td>
<td>72 (86)</td>
<td>69 (81)</td>
<td>77 (75)</td>
<td>77 (79)</td>
</tr>
<tr>
<td>Microbiologically evaluable‡</td>
<td>56 (67)</td>
<td>56 (66)</td>
<td>64 (62)</td>
<td>57 (58)</td>
</tr>
<tr>
<td>Patient Demographics (All Treated)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>44.6 ± 14.9</td>
<td>44.3 ± 14.5</td>
<td>44.7 (13.7)</td>
<td>42.3 (10.9)</td>
</tr>
<tr>
<td>Male</td>
<td>54 (64)</td>
<td>46 (55)</td>
<td>55 (55)</td>
<td>62 (65)</td>
</tr>
<tr>
<td>White</td>
<td>51 (61)</td>
<td>55 (66)</td>
<td>65 (65)</td>
<td>61 (64)</td>
</tr>
<tr>
<td>Predisposing Conditions</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Prior surgery</td>
<td>29 (35)</td>
<td>30 (36)</td>
<td>33 (33)</td>
<td>31 (33)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>25 (30)</td>
<td>19 (23)</td>
<td>18 (18)</td>
<td>14 (15)</td>
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<tr>
<td>Trauma</td>
<td>17 (20)</td>
<td>17 (21)</td>
<td>17 (17)</td>
<td>24 (25)</td>
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<tr>
<td>Skin diseases</td>
<td>4 (5)</td>
<td>2 (2)</td>
<td>5 (5)</td>
<td>5 (5)</td>
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<tr>
<td>Common Types of Infections</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abscess</td>
<td>39 (46)</td>
<td>41 (50)</td>
<td>58 (58)</td>
<td>55 (58)</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>29 (35)</td>
<td>32 (39)</td>
<td>29 (29)</td>
<td>27 (28)</td>
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<tr>
<td>Wound infection</td>
<td>11 (13)</td>
<td>8 (10)</td>
<td>11 (11)</td>
<td>10 (11)</td>
</tr>
<tr>
<td>Prior antibiotic treatment</td>
<td>67 (80)</td>
<td>56 (66)</td>
<td>69 (69)</td>
<td>61 (64)</td>
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<tr>
<td>Concomitant Antibiotic Treatment</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Aztreonam (Azactam)</td>
<td>29 (35)</td>
<td>24 (28)</td>
<td>41 (41)</td>
<td>35 (37)</td>
</tr>
<tr>
<td>Metronidazole (Flagyl)</td>
<td>20 (24)</td>
<td>21 (25)</td>
<td>44 (44)</td>
<td>36 (38)</td>
</tr>
</tbody>
</table>

* Patients with a confirmed diagnosis of a complicated skin and skin structure infection who received at least one dose of study medication.
† Patients in the all-treated population who complied with all exclusion and inclusion criteria and had a clinical response (cure or failure) at the test-of-cure visit.
‡ Patients in the clinically evaluable population who also had a baseline pathogen recovered from pre-treatment culture.
Clinical success rates were similar in FAST 2, which also compared telavancin with standard therapy. The all-treated population (n = 195) achieved cures as follows: 82 patients (82%) receiving telavancin and 81 patients (85%) in the standard therapy group (P = 0.37).

At the test-of-cure visit, the clinically evaluable population (n = 154) achieved cures as follows: 74 patients (96%) receiving telavancin and 72 patients (94%) receiving standard therapy (P = 0.37).

The ATLAS Trials

ATLAS 1 and 2 were two parallel-group, randomized, double-blind, active-control, phase 3 trials in which patients received either telavancin 10 mg/kg every 24 hours or vancomycin 1 g every 12 hours for suspected or confirmed gram-positive cSSSIs. The vancomycin dose was adjusted, when feasible, based on the standard practices of each individual institution and on each patient's CrCl. Oral antimicrobials were not permitted during the trial; however, if gram-negative or anaerobic coverage was required during the study period, using aztreonam with or without metronidazole was deemed appropriate.

Data from the ATLAS trials were pooled together for a total number of all-treated patients in the telavancin group (n = 745) and in the vancomycin group (n = 744). The telavancin group achieved an 88% cure rate, and the vancomycin group obtained a cure rate of 87%.

Baseline MRSA infections were documented in 53 patients in the all-treated group (86%) of the telavancin group and 75% of the standard-therapy patients achieved a cure.

At the baseline evaluation, cultured MRSA was noted in 53 patients in the all-treated group (n = 121). At the end of treatment, the infecting pathogen was judged to have been eradicated in 57 telavancin patients (89%) and in 44 standard-therapy patients (77%) (P = 0.09). At the end-of-treatment and follow-up visits, infection was eradicated in 94% of the patients receiving telavancin and in 83% of patients receiving standard therapy.

Microbiologically evaluable patients (n = 91) with isolated S. aureus at baseline demonstrated a cure rate of 96% with telavancin and a 90% cure rate with standard therapy. Eradication rates were 92% with telavancin and 78% with standard therapy (P = 0.07). The same cure rates (96% and 90%) were applied for the 45 patients in the microbiologically evaluable patients with isolated MRSA infection at baseline.

MRSA eradication rates with telavancin (96%) were significantly higher than with standard therapy (68%) (P = 0.04). Table 4 presents clinical responses at test-of-cure and follow-up visits in both FAST and FAST 2.
vancomycin. At the test-of-cure visit, the baseline pathogen had been eradicated in all patients.

Of those patients evaluated in the microbiologically evaluable group, documented MRSA infection was isolated at baseline in 579 patients and was eradicated at the test-of-cure evaluation in 90% of the telavancin group and in 85% of the vancomycin group. At the test-of-cure visit, pathogens were eradicated in 88% of the telavancin patients and in 86% of vancomycin patients. The therapeutic response for clinically evaluable patients was reported to be higher with telavancin (90%) than with vancomycin (85%). Patients who achieved cures at the test-of-cure visit in pooled analyses of ATLAS 1 and 2 are presented in Table 5.

**Summary**

The data reported from the FAST and ATLAS trials demonstrated the effectiveness and safety of telavancin in treating cSSSIs when compared with standard therapy or vancomycin. The results suggest that telavancin can be an option in treating these types of infections, particularly MRSA. Telavancin was more successful than standard therapy or vancomycin in achieving cures and in eradicating infection in these trials. In addition, overall cure rates with other problematic pathogens such as MSSA, *E. faecalis, S. pyogenes, S. agalactiae,* and *S. anginosus,* were similar between telavancin and standard therapy or telavancin and vancomycin. Telavancin was significantly superior to standard therapy in eradicating MRSA. These results suggest that telavancin might be a better treatment choice than other available agents.

**Pneumonia**

**ATTAIN 1 and ATTAIN 2**

The use of telavancin was evaluated in two identical randomized, double-blind, comparator-controlled, parallel-group phase 3 trials. Patients were men or non-pregnant women 18 years of age or older in 274 sites and 38 countries. Patients had clinical signs and symptoms of pneumonia, acquired either 48 hours after being in an inpatient setting or within seven days after discharge from a hospital stay of three days or more.

Patients received either telavancin 10 mg/kg every 24 hours or vancomycin 1 g every 12 hours for up to 21 days. Dose adjustments of both drugs were allowed based upon the patient’s CrCl. Patients with polymicrobial infections were allowed to receive concomitant therapy with aztreonam (Azactam) or piperacillin/tazobactam (Zosyn, Wyeth/Pfizer).

The primary efficacy endpoint for both ATTAIN trials was to assess the non-inferiority of telavancin to vancomycin. The secondary objective was to perform a pooled analysis of the superiority of telavancin over vancomycin in patients with a confirmed MRSA infection (the most common gram-positive pathogen isolated).

Pooled data suggested that cure rates among clinically evaluable patients were similar in treated patients (telavancin, 82%; vancomycin, 81%). The trials were completed and data were submitted as a New Drug Application (NDA) to the FDA in January 2009. Based on the data of the trials, however, efficacy was considered inconclusive in the treatment of nosocomial pneumonia because of insufficient evidence. The FDA requested further data in support of this indication.

**ADVERSE DRUG REACTIONS**

The more common adverse drug reactions associated with telavancin during clinical trials were nausea, vomiting, constipation, a metallic or soapy taste, headache, insomnia, pruritus, and foamy urine. Prolongation of the corrected QT (QTc) interval was also evident; however, this event was evaluated separately from other adverse events. Episodes of dyspnea were identified in patients with respiratory disease symptoms. Infusion-related reactions (e.g., “red man syndrome”) were also reported with telavancin use.

**Pregnancy**

Telavancin is classified as a Pregnancy Category C agent; however, the FDA issued a boxed warning concerning the potential risk for abnormal fetal development. The drug caused adverse developmental outcomes in three animal species, including reductions in fetal weight and digit and limb malformations in offspring.

Even though these findings were infrequent, the malformations in animals were noted at clinically relevant doses of telavancin. Consequently, women of childbearing age should undergo serum pregnancy testing before receiving this medication. Women who are not pregnant should be counseled on effective contraception during telavancin treatment. Telavancin should be avoided during all trimesters of pregnancy unless the benefits to the patient outweigh the potential risk to the fetus. Patients should notify their physician immediately if pregnancy is confirmed while they are receiving telavancin.

In order to collect pertinent information about telavancin use during pregnancy, Theravance has created a registry for physicians to register pregnant female patients eligible for telavancin therapy. Alternatively, women can enroll by calling 1-888-658-4228.

In lactating women who are breast-feeding, it is not clear whether telavancin is excreted in human breast milk. Caution in nursing mothers is advisable until further data become available.

### Table 5 Patients Achieving Cure at the Test-of-Cure Visit In a Pooled Analysis of ATLAS 1 and ATLAS 2

<table>
<thead>
<tr>
<th>Population</th>
<th>Telavancin Treatment (%)</th>
<th>Vancomycin Treatment (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 0017 (ATLAS 1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinically evaluable</td>
<td>304/346 (87.9)</td>
<td>302/349 (86.5)</td>
</tr>
<tr>
<td>All patients treated</td>
<td>323/426 (75.8)</td>
<td>321/429 (74.5)</td>
</tr>
<tr>
<td>Study 0018 (ATLAS 2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinically evaluable</td>
<td>354/399 (88.7)</td>
<td>346/395 (87.6)</td>
</tr>
<tr>
<td>All patients treated</td>
<td>387/502 (77.1)</td>
<td>375/510 (73.7)</td>
</tr>
<tr>
<td>Pooled Studies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinically evaluable</td>
<td>658/745 (88.3)</td>
<td>648/744 (87.1)</td>
</tr>
<tr>
<td>All patients treated</td>
<td>710/928 (76.5)</td>
<td>697/939 (74.2)</td>
</tr>
</tbody>
</table>
**Drug Forecast**

**Drug Interactions**

Significant drug–drug interactions have not been reported in the literature. Trials that evaluated the concomitant use of telavancin with midazolam (Versed, Roche), aztreonam, and piperacillin/tazobactam did not report any clinically relevant interactions between these agents, and no specific dosage adjustments were required.

Another noteworthy trial evaluated the effects of telavancin on cardiac repolarization using the electrocardiogram (ECG). In the study, 160 subjects received placebo, telavancin 7.5 mg/kg, or moxifloxacin (Avelox, Bayer) 15 mg/kg or 400 mg for three days. The mean effect on cardiac repolarization with telavancin was less than 5 msec with no dose correlation.

Although these findings suggest otherwise, telavancin should not be used in patients with congenital long QTc syndrome, prolongation of the QTc interval, uncompensated heart failure, or severe left ventricular hypertrophy. Another agent should be substituted for any medication that prolongs the QTc interval.

**Drug–Laboratory Interactions**

Telavancin does not necessarily interfere with coagulation itself, but some laboratory tests used in monitoring patients can be misinterpreted. Telavancin does interfere with the laboratory testing of prothrombin time, the International Normalized Ratio, activated partial thromboplastin time, activated clotting time, or factor Xa.

Clinical trials indicate no increased risk of bleeding with telavancin; nevertheless, test results were reported as falsely elevated when measured shortly after telavancin infusions. Therefore, blood samples in patients requiring coagulation testing should be collected before the dose of telavancin is given.

Other laboratory tests that do not appear to be affected by telavancin include thrombin time, bleeding time, D-dimer, fibrin-degradation products, functional (chromogenic) factor Xa, whole blood (Lee–White) clotting time, and ex vivo platelet aggregation.

**Contraindications**

No contraindications are listed in the prescribing information.

**Precautions and Warnings**

Nephrotoxicity has been noted with telavancin, with increased serum creatinine levels of up to 1.5 times baseline values reported. This event occurred more frequently with telavancin than with vancomycin in patients with normal baseline serum creatinine concentrations.

Nephrotoxicity was most likely to occur in patients with baseline comorbidities that predisposed them to kidney dysfunction (e.g., pre-existing renal disease, diabetes mellitus, congestive heart failure, or hypertension).

Co-administration of medications that affect renal function also predisposed patients to nephrotoxicity. Renal function should be monitored in all patients receiving telavancin during treatment at 48- to 72-hour intervals. More frequent monitoring may be necessary in patients with baseline comorbidities that can lead to further renal insufficiency. Patients with underlying renal insufficiency with a CrCl of 50 mL/minute or less had lower clinical cure rates than patients with a CrCl above 50 mL/minute.

Infusion-related reactions (e.g., red man syndrome) have been associated with telavancin treatment. Therefore, telavancin should be administered over 60 minutes to minimize the risk of infusion-related reactions, such as flushing of the upper body, urticaria, pruritus, or rash. If red man syndrome develops, slowing down or stopping the infusion terminates this reaction. Some cases of red man syndrome are more clinically significant when pharmacological intervention, such as fluids, antihistamines, corticosteroids, or vasopressor agents, is required.

As with most antimicrobials, the development of Clostridium difficile–associated diarrhea remains a growing concern. Telavancin is no exception when it comes to the development of this infection. Patients who are receiving telavancin or other antimicrobials, or both, who experience diarrhea should be evaluated for C. difficile infection and should be managed appropriately. Discontinuing the offending agent, instituting fluids and electrolyte management, and adding an agent used to treat C. difficile are recommended.

As is evident from trials conducted in healthy volunteers, doses of 7.5 and 15 mg/kg prolong the QTc interval; thus, telavancin should be used with caution in patients receiving other medications that prolong the QTc interval. Patients with congenital long QTc syndrome, a prolonged QTc interval, uncompensated heart failure, or severe left ventricular hypertrophy should be advised to avoid telavancin as a treatment option.

**Special Populations**

Telavancin is excreted primarily by the kidneys; therefore, dosing adjustments may be required for patients with renal insufficiency (a CrCl of 50 mL/minute or below). According to the manufacturer, patients with a CrCl of 30 to 49 mL/minute can receive telavancin 7.5 mg/kg every 24 hours. Patients with a CrCl of 10 to 29 mL/minute should receive telavancin 10 mg/kg every 48 hours. Information on dosing adjustments for those patients needing hemodialysis is limited.

Goldberg et al. evaluated telavancin in eight adults with moderate hepatic impairment (Child-Pugh Class B) and in a control group of healthy adults. The Crmax was reported to be 21% lower in patients with hepatic impairment; however, these results did not appear to be clinically significant. The study concluded that dose adjustments for patients with mild-to-moderate hepatic insufficiency are not needed. The significance of the drug’s effects in patients with severe hepatic impairment is not clear.

In another Goldberg study, single-dose pharmacokinetic parameters of telavancin 10 mg/kg were evaluated in 16 elderly patients. The mean clearance was 12.2 ± 1.4 mL/hour per kg. The half-life was 9.3 ± 1.3 hours, and the volume of distribution was 156 ± 12 mL/kg. Significant changes in these patients were not evident in this study; therefore, dosing adjustments in the geriatric population with normal renal function are not required.

**Dosage and Administration**

Vials of telavancin should be reconstituted with 5% dextrose, sterile water, or 0.9% sodium chloride. Following reconstitution, telavancin remains stable at room temperature for four to 12 hours. With refrigeration, it remains stable for three to seven days.

The recommended dose for the treat-
Telavancin should be prepared according to the product information.

No dosage adjustments are required for patients with mild-to-moderate hepatic impairment.

Because compatibility data are limited, mixing other intravenous (IV) medications simultaneously through the same IV line is not suggested. When drugs must be administered through the same line, flushing the line before and after telavancin infusion is recommended. Telavancin should be prepared according to the product information.

**P&T COMMITTEE CONSIDERATIONS**

Telavancin is the first lipoglycopeptide that has demonstrated good activity against gram-positive organisms. Advantages include its spectrum of activity, once-daily dosing without the need for therapeutic drug monitoring, and dual mechanism of action. However, the association with adverse events can limit its use in pregnant women and patients with kidney disease because of the elevated serum creatinine levels observed.

Baseline serum creatinine levels should be monitored before treatment and every 72 hours during therapy. Moreover, patients with uncompensated heart failure, severe left ventricular hypertrophy or who are at risk for QTc prolongation (or who are taking medications that prolong the QTc interval) should not receive telavancin.

As with vancomycin, infusing telavancin too quickly can cause red man syndrome. Telavancin is useful when other antimicrobials might promote resistance. More data are needed before P&T committees can decide whether to include telavancin on a hospital formulary. It will be challenging to determine this agent’s role in other types of infections.

**FUTURE TRENDS**

Besides telavancin, two lipoglycopeptides are on the horizon that might be even more efficacious. Dalbavancin (Pfizer) and oritavancin (The Medicines Company) are in development.

Based on preliminary data, differences between these agents are apparent in their terminal half-lives, which can permit infrequent dosing, thus reducing adverse events, minimizing the repetitive dosing of antibiotics, and potentially combating bacterial resistance. Dalbavancin has an exceedingly long half-life (approximately 250 hours), allowing for weekly dosing, and oritavancin has an even longer half-life (approximately 350 hours), possibly allowing for a single dose for a course of treatment. Oritavancin is eliminated hepatically, which can serve as an alternative route in patients with renal insufficiency.

**CONCLUSION**

Telavancin has a broad spectrum of antimicrobial activity against problematic gram-positive pathogens, including MRSA infection. This new antimicrobial entity can provide exceptional benefits compared with conventional therapies (i.e., convenient once-a-day dosing, the lack of a need for drug monitoring, concentration-dependent activity, bactericidal effects). All of these characteristics enable the drug to provide greater potency in eradicating pathogens and promoting a decline in bacterial resistance.

The new class of lipoglycopeptides should bring about major improvements in the arena of antimicrobials, with the potential to benefit patients with multidrug-resistant, gram-positive pathogens. Nonetheless, further evaluation and clinical monitoring of these agents are required to understand their role in clinical practice, especially in the era of bacterial resistance.

Telavancin’s spectrum of activity, its activity against vancomycin-resistant isolates of *S. aureus* (VRSA) and Van-B VRE, and its role in clinical practice make it a tremendously valuable agent, especially for patients with these complicated infections. Although telavancin is currently indicated only for treating cSSSIs, it will be interesting to observe the drug’s use in pneumonia, bacteremia, infective endocarditis, and other complicated infection processes.

**REFERENCES**

1. Telavancin (Vibativ), prescribing information. San Francisco/Deerfield, Ill.: Theravance/Astellas; September 2009.


