Tedizolid: The First Once-Daily Oxazolidinone Class Antibiotic

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Tedizolid phosphate is the second commercially available oxazolidinone antibiotic, although the first one in class that is dosed once daily. It is a prodrug that is rapidly converted to the active compound tedizolid. Tedizolid has activity against a wide range of gram-positive pathogens, including methicillin-resistant Staphylococcus aureus. It is approved to treat acute bacterial skin and skin structure infections (ABSSSIs). In 2 randomized controlled phase 3 trials, 6 days of tedizolid (200 mg once daily) has been proven to be noninferior to 10 days of linezolid (600 mg twice daily). These 2 ABSSSI studies have positioned tedizolid among the growing armamentarium of newer, novel, anti-gram-positive agents. Tedizolid appears to differ from linezolid in the incidence of gastrointestinal and hematologic side effects and appears to lack drug interactions with selective serotonin reuptake inhibitors. Conditions other than ABSSSI are currently being evaluated in clinical studies.

Keywords. tedizolid; oxazolidinone; linezolid; MRSA; ABSSSI.

Among the frequently encountered infectious diseases, skin and soft tissue infections (SSTIs) pose an exceedingly wide array of manifestations and can be caused by a similar broad range of etiologic agents. One of the most concerning aspects of these organisms are their unpredictable drug susceptibilities. A significant number of serious skin infections are due to Staphylococcus aureus, with variable fractions due to methicillin-resistant Staphylococcus aureus (MRSA). Vancomycin has traditionally been the workhorse drug for treatment of these serious MRSA infections. Beginning with its discovery in 1963, it was the antibiotic of choice for infections caused by MRSA. It was not until 1996 that the first vancomycin-intermediate S. aureus (VISA) isolate was described [1]. Over the next 19 years, VISA, heterogeneous VISA, and vancomycin-resistant S. aureus isolates have been described. In clinical practice, vancomycin failures are not uncommon and the etiology of these failures is variable, depending on the host and the pathogen being treated. Infectious Diseases Society of America guidelines exist both for the treatment of MRSA infections and for the diagnosis and management of SSTIs [2, 3]. However, since the development of these guidelines, several newer agents have been approved by the US Food and Drug Administration (FDA) for the treatment of acute bacterial skin and skin structure infections (ABSSSIs).

Tedizolid phosphate (formerly known as TR700 or torezolid) was approved on 20 June 2014, through an expedited review by the FDA after studies revealed it was noninferior to linezolid for the treatment of ABSSSIs. It is the first oxazolidinone to be approved since linezolid in 2000. In this article, we review the chemistry, mechanism of action, antimicrobial activity, pharmacodynamics, pharmacokinetics, clinical experience, and adverse events (AEs) of tedizolid. Finally, we hope to shed some light on the formulary issues involving tedizolid and its role in the anti-infective armamentarium.

CHEMISTRY

Tedizolid phosphate is a prodrug that is rapidly converted by endogenous phosphatases to tedizolid, the microbiologically active moiety. This rapid conversion
The D-ring of tedizolid is unique and is thought to contribute to additional hydrogen bonds and thus stronger binding at this site of activity [8–10]. Tedizolid distinguishes itself from linezolid by incorporating a D-ring substituent and a hydroxymethyl group in place of acetamide; both of these substitutions are important contributors to its clinical activity against some linezolid-resistant pathogens. The additional phosphate group of the prodrug increases the aqueous solubility, and thus bioavailability [4]. The D-ring provides more hydrogen bond interactions between tedizolid and the bacterial ribosome; thus, the drug is a more potent protein synthesis inhibitor than other oxazolidinones, and can therefore be given at much lower daily doses. The hydroxymethyl group causes less steric hindrance than the acetamide of linezolid in ribosomes that were methylated by the cfr (chloramphenicol-florphenicol resistance) enzyme (present in cfr-positive strains), a cause of linezolid-resistant gram-positive bacteria [5].

MECHANISM OF ACTION

According to in vitro studies, tedizolid is bacteriostatic against gram-positive organisms through inhibition of the early steps of bacterial protein synthesis. Interestingly though, some animal models suggest bactericidal activity in vivo [6]. Similar to linezolid, tedizolid exerts its activity by binding to the 23S ribosomal RNA of the 50S subunit, thereby preventing the formation of the 70S initiation complex and thus inhibiting protein synthesis [5,7,8]. The D-ring of tedizolid is unique and is thought to contribute to additional hydrogen bonds and thus stronger binding at this site of activity [8–10].

PHARMACOKINETICS

The oral bioavailability of tedizolid is >90%, and no dosage adjustment is necessary between intravenous and oral administration, nor is dosage adjustment needed based on hepatic or renal impairment or in the elderly [10–13]. The tedizolid half-life is approximately 12 hours, and steady-state concentrations are achieved within approximately 3 days. Peak plasma tedizolid concentrations are achieved within approximately 3 hours following oral administration under fasting conditions or at the end of the 1-hour intravenous infusion of tedizolid phosphate. Oral tedizolid phosphate may be administered with or without food. However, it was found in dose-range studies that the maximum concentration (C_{max}) and time to C_{max} (T_{max}) of tedizolid may be depressed when the oral drug was administered in the fed state. However, the overall absorption of tedizolid as measured by the area under the curve (AUC) was not altered by the subjects’ meal status [12]. Tedizolid is approximately 70%–90% protein bound. The volume of distribution of tedizolid in healthy adults following a single intravenous dose of tedizolid phosphate 200 mg ranged is 67–80 L. It is metabolized by sulfation, and the majority of elimination occurs via the liver, with 82% of the dose recovered in feces and 18% in urine, as an inactive sulfate metabolite [12–14]. This may limit its role in treating urinary tract infections. There is no effect on cytochrome P450 (CYP) enzymes, and no potential drug interactions with tedizolid were identified by in vitro CYP inhibition or induction studies [10].

Tedizolid is a reversible inhibitor of monoamine oxidase (MAO) in vitro. The interaction with MAO inhibitors could not be evaluated in phase 2 and 3 trials, as subjects taking such medications were excluded. Preclinical studies suggest that, compared with linezolid, there will be less MAO inhibition and therefore fewer drug interactions with serotonergic and adrenergic agents. Although patients on selective serotonin reuptake inhibitors (SSRIs) were excluded from clinical trials, it is not expected that serotonin syndrome will be an issue when tedizolid is coadministered with these medications. This interaction was evaluated using the murine head twitch model, a method used to evaluate serotonergic activity of antidepressant medications for decades. Mice were treated with human therapeutic equivalents of tedizolid (4 different doses with the maximum 30 times the human equivalent dose), linezolid, moclobemide (reversible MAO-A inhibitor), and fluoxetine. Linezolid, fluoxetine, and moclobemide significantly increased the number of mouse head twitches, signifying increased serotonergic activity. In contrast, tedizolid did not increase the head twitch response at any administered dose, suggesting no increase in serotonin activity with the drug [15]. With this model, there was no evaluation of tedizolid in combination with fluoxetine or other SSRIs.

Tedizolid has been found to accumulate in both peripheral blood and alveolar macrophages (AMs) [4,16–20]. It is highly concentrated in lung epithelial lining fluid (ELF) and lung AMs, with a ratio of 20-fold relative to the free drug in the plasma [17]. Although ongoing human studies in treating nosocomial pneumonia with tedizolid have not yet been completed,
mouse model and healthy human volunteer ELF and AM concentration data suggest that these pharmacodynamic characteristics of tedizolid are favorable [4, 16–20].

PHARMACODYNAMICS AND ANTIMICROBIAL ACTIVITY

Tedizolid has broad gram-positive activity, including activity against many resistant organisms. Preclinical data and clinical data from isolates gathered in phase 2 and 3 clinical studies are summarized in Table 1. In brief, tedizolid is approved for the treatment of ABSSSIs caused by S. aureus (including MRSA and methicillin-susceptible S. aureus [MSSA] isolates), Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus anginosus group (including Streptococcus anginosus, Streptococcus intermedius, and Streptococcus constellatus), and Enterococcus faecalis. It also has in vitro activity against other gram-positive organisms typically causing ABSSSIs—namely, coagulase-negative staphylococci, less common streptococci, Corynebacterium jeikeium, and Enterococcus faecium (including VRE). Aside from these gram-positive skin pathogens, tedizolid also has in vitro activity against some atypical organisms, some atypical mycobacteria, and some anaerobic organisms [21–26].

With tedizolid, the AUC/minimum inhibitory concentration (MIC) is the pharmacodynamic parameter that best predicts tedizolid activity in animal infection models [10, 16]. When compared with linezolid, multiple studies have repeatedly demonstrated lower tedizolid MIC50 and MIC90 (MIC required to inhibit growth of 50 and 90% of organisms) for staphylococci, enterococci, and streptococci [21, 25–28, 30, 31]. Tedizolid is 4- to 16-fold more potent in vitro than linezolid against many clinically relevant pathogens [21, 25, 27, 30]. Relative MIC data are found in Table 1. When evaluating these susceptibility data, it is important to understand that while linezolid MICs may be higher than tedizolid, the AUC for linezolid is at least twice that of tedizolid (when they are prescribed at approved doses). The clinical significance is that similar AUC/MIC ratios may be obtainable with less total tedizolid drug exposure and potentially less cumulative toxicity.

Development of linezolid resistance typically requires multiple mutations of the redundant chromosomal genes for the 23S ribosomal subunit. Most gram-positive bacteria have 4–6 copies of this gene, making intrinsically mutated 23S subunits a poor mechanism of resistance [28, 30–33]. However, the plasmid-encoded chloramphenicol resistance gene cfr confers resistance to linezolid, as well as other inhibitors of protein synthesis (including chloramphenicol, clindamycin, and quinupristindalfopristin) through modification of the drug ribosome binding sites. Tedizolid appears to retain in vitro activity against some linezolid-resistant S. aureus, coagulase-negative staphylococci, and enterococci, in particular staphylococci harboring the resistance gene cfr [26, 29, 33]. However, if the plasmid-mediated cfr gene is present with chromosomally mediated linezolid resistance, tedizolid resistance is likely. In the largest surveillance study to date, resistance to tedizolid was found in 13 of 6884 (0.002%) gram-positive bacteria, and all 13 were also resistant to linezolid [28]. In the Efficacy and Safety of 6-Day Oral Tedizolid in Acute Bacterial Skin and Skin Structure Infections vs 10-

Table 1. Microbiologic Data

<table>
<thead>
<tr>
<th>Organism</th>
<th>MIC50</th>
<th>MIC90</th>
<th>CLSI Breakpoints</th>
<th>Resistant</th>
<th>MIC50</th>
<th>MIC90</th>
<th>CLSI Breakpoints</th>
<th>Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>0.25</td>
<td>0.25–0.5</td>
<td>&lt;0.5</td>
<td>≥2</td>
<td>2</td>
<td>2</td>
<td>&lt;4</td>
<td>≥8</td>
</tr>
<tr>
<td>MSSA</td>
<td>0.25</td>
<td>0.25–0.5</td>
<td>&lt;0.5</td>
<td>≥2</td>
<td>2</td>
<td>2</td>
<td>&lt;4</td>
<td>≥8</td>
</tr>
<tr>
<td>MRSA</td>
<td>0.25</td>
<td>0.25–0.5</td>
<td>&lt;0.5</td>
<td>≥2</td>
<td>2</td>
<td>2</td>
<td>&lt;4</td>
<td>≥8</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>0.12</td>
<td>0.25</td>
<td>≤0.05</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>≤2</td>
<td></td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>0.12</td>
<td>0.25</td>
<td>≤0.05</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>≤2</td>
<td></td>
</tr>
<tr>
<td>Streptococcus pneumonia</td>
<td>0.25</td>
<td>0.25</td>
<td>≤0.05</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>≤2</td>
<td></td>
</tr>
<tr>
<td>Streptococcus agalactiae</td>
<td>0.25</td>
<td>0.25</td>
<td>≤0.05</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>≤2</td>
<td></td>
</tr>
<tr>
<td>Streptococcus anginosus group</td>
<td>0.25</td>
<td>0.25</td>
<td>≤0.05</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>≤2</td>
<td></td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>0.25</td>
<td>0.5</td>
<td>≤0.05</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>≤2</td>
<td>≥8</td>
</tr>
<tr>
<td>Enterococcus faecium</td>
<td>0.25</td>
<td>0.5</td>
<td>≤0.05</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>≤2</td>
<td>≥8</td>
</tr>
<tr>
<td>Linezolid-resistant CoNS</td>
<td>2</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linezolid-resistant enterococci</td>
<td>0.5</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as µg/mL.

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; CoNS, coagulase-negative staphylococci; MIC, minimum inhibitory concentration; MIC50, MIC required to inhibit 50% of the isolates; MIC90, MIC required to inhibit 90% of the isolates; MRSA, methicillin-resistant Staphylococcus aureus; MSSA, methicillin-sensitive Staphylococcus aureus.
Day Oral Linezolid Therapy (ESTABLISH) 1 and 2 studies, the highest MIC found in any *S. aureus* isolate was 0.5 µg/mL [24, 34].

**CLINICAL EXPERIENCE**

**Acute Bacterial Skin and Skin Structure Infection**

**Phase 2 Study**

In the first clinical treatment trial, patients with complicated skin and skin structure infections were randomized to receive 200 mg, 300 mg, or 400 mg per day of tedizolid for 5–7 days. The primary endpoint was clinical response at the test-of-cure visit (7–14 days after treatment). Of 188 patients, 76.6% were diagnosed with an abscess, 17.6% had cellulitis, and 5.9% had a wound infection. Due to the high incidence of abscesses, 154 had culture positive results, of which 139 had *S. aureus* (80.6% were MRSA). Cure rates were 96.6% for all *S. aureus*, and 96.8% for MRSA. At the end of therapy, there were no significant differences between the treatment groups, and the overall cure rates were 95.7% in the clinically evaluable (CE) group and 87.8% in the modified intention-to-treat group [22].

**Phase 3 Studies**

**ESTABLISH-1.** ESTABLISH-1 [24] was a randomized, double-blind, noninferiority trial. The primary efficacy outcome was early clinical response at 48–72 hours, defined as no increase in lesion surface area from baseline and an oral temperature <37.6°C, confirmed by a second temperature measurement within 24 hours of the 48- to 72-hour assessment. The median area of infection was 188.3 cm² in the tedizolid arm and 190.0 cm² in the linezolid arm. Wound infections accounted for 30% of the patients; abscesses occurred in 30%, whereas 40% experienced cellulitis. A bacterial etiology was identified in approximately 63% (31% of cellulitis patients compared with 85% in patients with abscesses), with *S. aureus* accounting for nearly 82% (MRSA, 42.5%). Of the 332 patients in the tedizolid arm, 79.5% had an early clinical response, whereas 79.4% of the 335 patients in the linezolid arm experienced an early clinical response. Sustained clinical response at the end of treatment (day 11) was 69.3% with tedizolid and 71.9% with linezolid. All secondary measures with tedizolid were noninferior. The clinical response rate at the posttherapy evaluation (1–2 weeks after the end of treatment) was 85.5% with tedizolid and 86% with linezolid [24].

**ESTABLISH-2.** The ESTABLISH-2 randomized, double-blind, noninferiority trial compared 6 days of intravenous-to-oral tedizolid 200 mg daily with 10 days of intravenous-to-oral linezolid 600 mg every 12 hours in adult patients with ABSSSI [34]. The primary outcome was >20% reduction in the area of infection at 48–72 hours. Wound infections accounted for 30%; abscesses occurred in 20%, whereas 50% experienced cellulitis. With tedizolid, the median area of infection was 231.3 cm² compared with 238.6 cm². Gram-positive organisms were isolated in 60%, of which 27% were MRSA, 53% were MSSA, and 13% were *β*-hemolytic streptococci. Early clinical response was found in 85% of the tedizolid group and 83% of the linezolid group. Clinical response rates at the posttherapy evaluation (1–2 weeks after the end of treatment visit) were 88% with tedizolid and 89% with linezolid [34, 35].

In both ABSSSI studies, the response rates with *Streptococcus anginosus* (milleri) group were numerically lower with linezolid (70% vs 89%). Clinical significance of this is unknown at this time, as the numbers in both arms were small and subgroup analysis on these patients is not available [24, 34].

**SPECIAL GROUPS**

**Obesity**

Pooled data from ESTABLISH-1 and -2 reveal that 200 (30%) of enrolled patients in the tedizolid arm had a body mass index (BMI) >30 kg/m² compared with 232 (35%) in the linezolid arm [24, 34]. ESTABLISH-1 patients with a BMI >40 kg/m² were excluded but could be included in ESTABLISH-2. Observed plasma levels were similar for obese and nonobese patients. Early clinical response rates in patients with a BMI >35 kg/m² were lower with tedizolid compared with linezolid (72.6% vs 84.9%), although the rate of clinical success in CE analysis was similar between the 2 arms (unpublished data, Cubist Pharmaceuticals).

**Diabetes**

Data from ESTABLISH-1 and -2 demonstrated lower early response to therapy with tedizolid in patients with diabetes. Clinical response was seen in the first 48–72 hours in 70.7% and 82.1% of diabetic subjects who received tedizolid and linezolid, respectively. Posttherapy evaluations revealed clinical similar findings with responses to therapy documented in 84.3% and 94.7%, respectively [24, 34]. While there was an overlap between diabetic patients and patients with a BMI >35 kg/m², no apparent explanation could be found for the differences.

**Bacteremia**

Analysis of ESTABLISH-1 and -2 identified bacteremia in 11 patients in the tedizolid arm and 16 patients in the linezolid arm [24, 34, 35]. Patients with staphylococcal bacteremia were stratified into high- and low-risk groups (based on echocardiographic results, presence of prosthetic material, and repeat culture results), and only low-risk patients could be enrolled in the studies at the investigators’ discretion. In total, 11 of 11 patients (2 MRSA, 4 MSSA, and 5 non-*S. aureus*) in the tedizolid arm, whereas 11 of 16 patients in the linezolid arm (6 MRSA, 3 MSSA and 7 non-*S. aureus*) responded. Enrolled bacteremic patients were treated per protocol and received no extension in
duration of therapy. An individual analysis of these 27 patients was not performed (unpublished data, Cubist Pharmaceuticals).

**Other Clinical Conditions**

A phase 3 study is under way comparing 7 days of tedizolid with 10 days of linezolid for treatment of ventilated patients with presumed gram-positive health-care associated pneumonia or ventilator-associated pneumonia. There are no studies or case reports currently available on the use of tedizolid to treat urinary tract infections.

**Adverse Events**

The safety and tolerability of tedizolid has been evaluated in the phase 2 trial as well as in ESTABLISH-1 and -2. (Table 2) In the phase 2 study, no patients discontinued treatment due to an AE; however, 69% of the patients did report a treatment-emergent AE (72.3% were graded as mild and 24.6% as moderate in severity). Dose-related toxicity was not apparent. Gastrointestinal (GI) side effects and headache were the most common AE. No significant thrombocytopenia or cardiac AEs were reported [11].

With ESTABLISH-1 and -2, median time to adverse reactions was 5 days for both arms, GI side effects were most frequently reported in both arms, including nausea, diarrhea, and vomiting (Table 2). Diarrhea was rated as mild in 84.6% and 85.7% and moderate in 15.4% and 14.3% of patients with tedizolid and linezolid, respectively. GI side effects with tedizolid were noted to be lower in all subgroups analyzed, with the exception of patients with moderate-to-severe renal insufficiency. The decreased incidence of GI side effects with tedizolid is likely due to the once-daily dosing rather than duration of exposure [24, 34, 35].

Hematologic side effects with linezolid have always been of concern, especially with prolonged courses of therapy. A phase 1 study with healthy volunteers demonstrated no hematologic side effects with any cell line after 21 days of tedizolid 200 mg daily [37]. ESTABLISH-1 and -2 suggest that tedizolid confers a lower potential for reduced platelets than does linezolid [24, 34, 36]. Data are lacking regarding the hematologic side effects beyond the 6 days of therapy in the ESTABLISH trials and in populations with conditions other than ABSSSIs. The hematologic side effects from both drugs are provided in Table 2. No bleeding AEs were noted [24, 34, 35]. The difference in platelet effects of the 2 drugs may be related to mitochondrial toxicity associated with free-plasma concentrations or may be due to shorter courses of therapy.

**Formulary Issues/Role in Armamentarium**

Oral and intravenous tedizolid costs US$235 per day. The cost for linezolid varies by route of administration and whether branded or generic versions are utilized. Branded intravenous linezolid (Zyvox) is currently available for $288 per day, whereas branded oral linezolid (Zyvox) costs $246 per day. Generic intravenous linezolid is currently less costly than tedizolid, oral linezolid, and branded linezolid (intravenous or oral).

As hospitals discuss the pharmaceutical formulary role of tedizolid, there are several advantages to be considered. The apparent lack of interactions with SSRIs can be a significant benefit. Healthcare providers may not feel comfortable prescribing linezolid in patients who are receiving SSRIs due to the FDA warning, especially to patients who are receiving multiple psychotropic medications. However, prescribers must keep in mind that the lack of an interaction between tedizolid and SSRIs are currently lacking clinical confirmation, as no patients in ESTABLISH-1 and -2 were on concomitant SSRIs due to the black-box warning with the comparator, linezolid. Postmarketing data will need to be collected to clarify this clinical entity, as serotonin syndrome is rare and could not be studied prospectively. Author (S. D. B.) experience with tedizolid has demonstrated fewer GI side effects, including patients who have had

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**Table 2. Comparison of Adverse Events With Tedizolid and Linezolid From the ESTABLISH Studies**

<table>
<thead>
<tr>
<th>TEAEs</th>
<th>Tedizolid 200 mg Daily (n = 618)</th>
<th>Linezolid 600 mg Twice Daily (n = 617)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinued due to adverse event</td>
<td>3 (0.5)</td>
<td>6 (0.9)</td>
</tr>
<tr>
<td>At least 1 serious adverse events</td>
<td>12 (1.8)</td>
<td>13 (2)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>106 (16)*</td>
<td>152 (23)</td>
</tr>
<tr>
<td>Nausea</td>
<td>54 (8)*</td>
<td>81 (12)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>19 (2.9)*</td>
<td>37 (5.6)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>26 (3.9)</td>
<td>35 (5.3)</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>4 (0.6)</td>
<td>8 (1.2)</td>
</tr>
<tr>
<td>Hematologic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb &lt;10.1 g/dL in males, &lt;9 g/dL in females</td>
<td>19 (3.1)</td>
<td>23 (3.7)</td>
</tr>
<tr>
<td>ANC &lt;800 cells/µL</td>
<td>3 (0.5)</td>
<td>4 (0.6)</td>
</tr>
<tr>
<td>Platelets &lt;112 500 cells/µL</td>
<td>7 (1.3)</td>
<td>20 (3.7)</td>
</tr>
<tr>
<td>Neurologic</td>
<td>65 (9.8)</td>
<td>67 (10.1)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>12 (1.8)</td>
<td>14 (2.1)</td>
</tr>
<tr>
<td>Headache</td>
<td>41 (6.2)</td>
<td>39 (5.9)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>10 (1.5)</td>
<td>5 (0.8)</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>8 (1.2)</td>
<td>4 (0.6)</td>
</tr>
<tr>
<td>Optic nerve disorders</td>
<td>2 (0.3)</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Dermatologic</td>
<td>47 (7.1)</td>
<td>40 (6)</td>
</tr>
<tr>
<td>Generalized pruritus</td>
<td>11 (1.7)</td>
<td>7 (1.1)</td>
</tr>
</tbody>
</table>

Data are presented as No. (%).

**Abbreviations:** ANC, absolute neutrophil count; ESTABLISH, Efficacy and Safety of 6-Day Oral Tedizolid in Acute Bacterial Skin and Skin Structure Infections vs 10-Day Oral Linezolid Therapy; Hb, hemoglobin; TEAE, treatment-emergent adverse event.

* P < .05.

Source: [24, 34, 36].

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**At least 1 serious adverse event discontinued due to adverse event.**
previous GI intolerance with linezolid. Although its high bioavailability limits the role for outpatient intravenous infusions, there may be select outpatient antibiotic therapy situations where its daily dosing is beneficial. Last, tedizolid does offer a treatment option for some linezolid-resistant gram-positive bacteria.

Linezolid does maintain certain advantages over tedizolid to date, including its FDA indication for pneumonia (nosocomial and community acquired), complicated skin and skin structure infections (including diabetic foot infections without concomitant osteomyelitis), and uncomplicated skin and skin structure infections, as well as for VRE. Some physicians are comfortable with prolonged courses of linezolid with close clinical monitoring, whereas the longest use of tedizolid to date is 21 days in healthy subjects.

Tedizolid offers clinicians once-daily gram-positive antibiotic coverage available in intravenous formulation or orally with excellent bioavailability. Although it does offer many of the same benefits as linezolid, unique to tedizolid are its lack of SSRI interaction, activity against many linezolid-resistant *S. aureus* isolates, and seemingly better side effect profile, at least in short-term administration. Efforts to expand our clinical knowledge into other disease processes such as pneumonia are critical to help practicing physicians determine where this drug fits into the antibiotic armamentarium.

**Note**

**Potential conflict of interest.** S. D. B. has served on the speakers’ bureaus for Cubist and Merck. R. T. has served on the speakers’ bureaus for Cubist and Sanofi Pasteur.

Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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