

## **Class Review: Oxazolidinone Antibiotics**

**Month/Year of Review:** May 2015

### **Research Questions:**

- What is the evidence of efficacy or effectiveness for linezolid versus tedizolid for treatment of the following infections caused by susceptible gram-positive bacteria: nosocomial pneumonia, community acquired pneumonia, complicated or uncomplicated skin and skin structure infections (including diabetic foot infections without concomitant osteomyelitis) or vancomycin-resistant *Enterococcus faecium* (VRE) infections.
- What is the evidence of harms for linezolid versus tedizolid for treatment of the following infections caused by susceptible gram-positive bacteria: nosocomial pneumonia, community acquired pneumonia, complicated or uncomplicated skin and skin structure infections (including diabetic foot infections without concomitant osteomyelitis) or VRE infections.
- Is there evidence for specific patient populations or sub-groups where linezolid or tedizolid would be more effective or less harmful for treatment of the following infections caused by susceptible gram-positive bacteria: nosocomial pneumonia, community acquired pneumonia, complicated or uncomplicated skin and skin structure infections (including diabetic foot infections without concomitant osteomyelitis) or VRE infections.

### **Conclusions:**

- No evidence was identified to support the use of tedizolid for treatment of nosocomial pneumonia or community acquired pneumonia caused by gram-positive bacteria. No evidence was identified to support the use of tedizolid for treatment VRE infections.
- There is moderate quality evidence from 2 good quality randomized active control trials (n=1333) that tedizolid is non-inferior to linezolid for treatment of complicated skin and skin structure infections (excluding diabetic foot infections).
- There is insufficient evidence from 2 good quality randomized active control trials to evaluate differences in harms between tedizolid and linezolid.
- Tedizolid has not been evaluated in an adequate numbers of children or elderly patients.

### **Recommendations:**

- Create a new Preferred Drug List Oxazolidinone Antibiotics Class including linezolid and tedizolid.
- Prefer linezolid because of proven benefit for multiple indications caused by susceptible gram-positive bacteria: nosocomial pneumonia, community acquired pneumonia, complicated or uncomplicated skin and skin structure infections (including diabetic foot infections without concomitant osteomyelitis) or vancomycin-resistant *Enterococcus faecium* (VRE) infections.
- Recommend implementing prior authorization criteria to restrict use of tedizolid to complicated skin and skin structure infections or other infections caused by gram-positive bacteria and not susceptible to other first-line therapies (see Appendix 3).

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**Purpose for Class Review:**

Linezolid was approved in April 2000 and tedizolid was approved June 2014 as a second drug in the oxazolidinone class. The goal of this review is to compare both drugs for effectiveness and harms and to consider their potential management via the Preferred Drug List.

**Background:**

Linezolid was approved in April 2000 under a Food and Drug Administration (FDA) priority review based upon 9 unpublished controlled clinical trials of more than 4000 patients.<sup>1</sup> It was the first drug in a new class and only the second drug approved to treat vancomycin-resistant *Enterococci* (VRE). It is indicated for both adults and children and for several infections caused by susceptible gram-positive bacteria (Table 1). Its role has been primarily for multiple drug resistant organisms (e.g. methicillin-resistant *Staphylococcus aureus* [MRSA] and VRE). Vancomycin is the “gold standard” treatment for MRSA but there is some emergence of less-susceptible strains, increased nephrotoxicity with the higher doses and it is not orally bioavailable. Tedizolid was approved June 2014 for use only for adults for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible bacteria.

Nosocomial pneumonia can be associated with various pathogens and varies across hospitals and time frames. MRSA is one of the most common causes.<sup>2</sup> The Infectious Diseases Society of America recommends vancomycin or linezolid as first-line treatment for nosocomial pneumonia caused by MRSA.<sup>3</sup> *Streptococcus pneumoniae* is the most common community acquired pneumonia pathogen<sup>4</sup> but MRSA has been associated with 2.4% cases in a recent prospective cohort study.<sup>5</sup> Linezolid or vancomycin is recommended for community acquired pneumonia cases caused by confirmed MRSA.<sup>4</sup> VRE is often resistant to multiple antibiotic classes and this is a concern because the incidence is increasing in the United States.<sup>6</sup> VRE can infect multiple sites. Linezolid and daptomycin are recommended for strains not susceptible to ampicillin.

The FDA has defined acute bacterial skin and skin structure infections (ABSSSI) as a bacterial infection of the skin with a lesion size area of at least 75 cm<sup>2</sup> (lesion size measured by the area of redness, edema, or induration). ABSSSIs include major cutaneous abscess, cellulitis and wound infections. It is estimated that approximately 45 – 60% of skin abscesses, 50% of purulent cellulitis, and >50% of purulent wounds are due to MRSA.<sup>7,8</sup> Linezolid is recommended empirically as a first-line alternative to vancomycin only for severe abscesses or purulent skin infections due to susceptible MRSA.<sup>9</sup> Linezolid is an effective oral alternative to vancomycin. Myelosuppression (anemia, thrombocytopenia, leukopenia and pancytopenia) have been reported during clinical trials of linezolid.<sup>10</sup> Tedizolid is a second generation oxazolidinone active against all clinically relevant gram-positive pathogens, is also available orally and intravenously but has only been evaluated for ABSSSI.

A summary of relevant drug information is available in **Appendix 1**, which includes pharmacology and pharmacokinetic characteristics of these drugs, contraindications, warnings and precautions, including any Black Boxed Warnings and Risk Evaluation Mitigation Strategies.

**Table 1. Indications and Dosing**

| Drug Name (Manufacturer)                         | Indication(s)  | Strength  | Dose, Route and Frequency  |
|--|--|---|--|
| linezolid (Pfizer) <sup>10</sup>                 | Treatment of the following infections caused by susceptible Gram-positive bacteria:<br>1) Nosocomial pneumonia<br>2) Community acquired pneumonia<br>3) Complicated or uncomplicated skin and skin structure infections (including diabetic foot infections without concomitant osteomyelitis)<br>4) Vancomycin-resistant <i>Enterococcus faecium</i> infections | - 600 mg film-coated tablets<br>- 100 mg/5mL powder for oral suspension<br>- 2 mg/mL (200 and 600 mg) in sterile isotonic solution for intravenous infusion | Adults:<br>- 600 mg PO or IV Q12H<br>Pediatrics:<br>- 10 mg/kg PO or IV Q8H<br>Pediatric skin infections:<br>< 5 yrs.: 10 mg/kg PO Q8H; 5-11 yrs.: 10 mg/kg PO Q12H; >11 years: 600 mg PO Q12H<br><br>x 10 – 28 days (varies by site & organism) |
| tedizolid (Cubist Pharmaceuticals) <sup>11</sup> | Treatment of acute bacterial skin and skin structure infections caused by designated susceptible bacteria.   | - 200 mg tablet<br>- 200 mg powder for reconstitution for IV infusion   | Adults:<br>- 200 mg PO or IV Q24H x 6 days   |

Abbreviations: MDRSP = multidrug-resistant *Streptococcus pneumoniae*; MRSA = methicillin-resistant *Staphylococcus aureus*; PO = oral; IV = intravenous; Q = every; H = hours

### Methods:

A Medline literature search for new systematic reviews and randomized controlled trials (RCTs) assessing clinically relevant outcomes to placebo or active controls were conducted. The Medline search strategy used for this review is available in **Appendix 2**, which includes dates, search terms and limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), Cochrane Collection, National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, BMJ Clinical Evidence, Dynamed, and the Canadian Agency for Drugs and Technologies in Health (CADTH) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drugs, indications, and safety alerts. Finally, the AHRQ National Guideline Clearinghouse (NGC) was searched for updated and recent evidence-based guidelines. The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources. No randomized controlled trials were found that evaluated tedizolid for nosocomial pneumonia, community acquired pneumonia or VRE. As such, this review will focus only comparisons of linezolid to tedizolid for ABSSSI.

**Table 2. Summary of Pivotal Studies Completed**

| Study  | Comparison   | Population  | Primary Outcome                          | Results  | Quality* |
|--|--|---|--|--|----------|
| ESTABLISH-1 <sup>12</sup><br>(Phase-3, RCT, DB, MC, non-inferiority) | tedizolid 200 mg po QDay x 6 days vs. linezolid 600 mg po Q12H x 10 days   | Adults with complicated ABSSSI caused by MRSA or other gram positive organisms                  | Clinical response @ the 48-72 assessment | <u>ITT</u><br>T: 264/332 (79.5%)<br>L: 266/335 (79.4%)<br>ARR: 0.1% 95% CI: -6.1 to 6.2 (within Δ of -10%)<br><br><u>PP at end of treatment</u><br>T: 219 / 273 (80.2%)<br>L: 232 / 286 (81.1%)<br>ARR: -0.9% 95% CI: -7.7 to 5.4 (within Δ of -10%)     | Good     |
| ESTABLISH-2 <sup>13</sup><br>(Phase-3, RCT, DB, MC, non-inferiority) | tedizolid 200 mg IV QDay x 6 days vs. linezolid 600 mg IV Q12H x 10 days<br><br>step down to oral allowed after 2 days if met criteria | Patients aged ≥15 years with complicated ABSSSI caused by MRSA or other gram positive organisms | Clinical response @ the 48-72 assessment | <u>ITT</u><br>T: 283 / 332 (85.2%)<br>L: 276 / 334 (82.6%)<br>ARR: 2.6% 95% CI: -3.0 to 8.2 (within Δ of -10%)<br><br><u>PP at end of treatment</u><br>T: 268 / 290 (92.4%)<br>L: 269 / 280 (96.1%)<br>ARR: -3.7% 95% CI: -7.7 to 0.2 (within Δ of -10%) | Good     |

Abbreviations: ABSSSI = acute bacterial skin and skin structure infections; DB = double-blind; ITT = intention-to-treat; H = hours; MC = multi-center; MRSA = methicillin-resistant *Staphylococcus aureus*; PP= per protocol; Q = every; RCT = randomized controlled trial. \*Quality of each study is ranked as “Good”, “Fair” or “Poor” based on DURM Standard Methods for Quality Assessment and Grading the Evidence.

**Systematic Reviews:**

None identified that included both linezolid and tedizolid.

**Guidelines:**

The Infectious Diseases Society of America published updated practice guidelines for the diagnosis and management of skin and soft tissue infections in June 2014.<sup>9</sup> The guidelines used a systematic GRADE approach to weigh the strength of recommendations and quality of the evidence. Linezolid is a recommended alternative to vancomycin for serious purulent skin and soft tissue infections caused by MRSA.<sup>9</sup> Tedizolid was not reviewed for the guidelines.

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## References:

1. Linezolid (Zyvox). *The Medical Letter on Drugs and Therapeutics*. 2000;42(W1079A):45-47.
2. Jones RN. Microbial etiologies of hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia. *Clin Infect Dis*. 2010;51 Suppl 1:S81-S87. doi:10.1086/653053.
3. Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. *Clin Infect Dis*. 2011;52(3):e18-e55. doi:10.1093/cid/ciq146.
4. Said MA, Johnson HL, Nonyane BAS, et al. Estimating the burden of pneumococcal pneumonia among adults: a systematic review and meta-analysis of diagnostic techniques. *PLoS ONE*. 2013;8(4):e60273. doi:10.1371/journal.pone.0060273.
5. Moran GJ, Krishnadasan A, Gorwitz RJ, et al. Prevalence of methicillin-resistant *Staphylococcus aureus* as an etiology of community-acquired pneumonia. *Clin Infect Dis*. 2012;54(8):1126-1133. doi:10.1093/cid/cis022.
6. Vancomycin-resistant enterococci (VRE) infection. In: *DynaMed [online Database]*. 2014th ed. United States: EBSCO Information Services; 2014. <http://web.b.ebscohost.com.liboff.ohsu.edu/dynamed/detail?vid=14&sid=e137b987-275c-41aa-8f18-113fca76ebf1%40sessionmgr114&hid=116&bdata=JnNpdGU9ZHluYW1lZC1saXZlJnNjb3BIPXNpdGU%3d#db=dme&AN=193562>. Accessed March 13, 2015.
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8. Moran GJ, Krishnadasan A, Gorwitz RJ, et al. Methicillin-resistant *S. aureus* infections among patients in the emergency department. *N Engl J Med*. 2006;355(7):666-674. doi:10.1056/NEJMoa055356.
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10. Zyvox Label. Pfizer. 2013. [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2014/021130s032,021131s026,021132s031lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/021130s032,021131s026,021132s031lbl.pdf). Accessed March 13, 2015.
11. Sivextro Label. Cubist Pharmaceuticals. 2015. [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2015/0205435s001,0205436s001lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/0205435s001,0205436s001lbl.pdf). Accessed March 13, 2015.
12. Prokocimer P, De Anda C, Fang E, Mehra P, Das A. Tedizolid phosphate vs linezolid for treatment of acute bacterial skin and skin structure infections: The establish-1 randomized trial. *JAMA*. 2013;309(6):559-569. doi:10.1001/jama.2013.241.
13. Moran GJ, Fang E, Corey GR, Das AF, De Anda C, Prokocimer P. Tedizolid for 6 days versus linezolid for 10 days for acute bacterial skin and skin-structure infections (ESTABLISH-2): a randomised, double-blind, phase 3, non-inferiority trial. *The Lancet Infectious Diseases*. 2014;14(8):696-705. doi:10.1016/S1473-3099(14)70737-6.

## Appendix 1: Specific Drug Information

**Table 3. Clinical Pharmacology and Pharmacokinetics**

| Drug Name               | Mechanism of Action   | Absorption   | Metabolism/Excretion  | Pharmacokinetics (mean)   |
|-------------------------|---|--|---|---|
| linezolid <sup>10</sup> | - binds to bacterial 23S ribosomal RNA of the 50S subunit<br>- prevents formation of a functional 70S initiation complex (an essential component of the bacterial translation process)<br>- bacteriostatic against enterococci and staphylococci.<br>- bactericidal for majority of streptococci isolates | ~ 100% orally bioavailable<br><br>- not affected by food | - primarily oxidated resulting in two inactive metabolites.<br>- In vitro studies suggest minimal P450 metabolism but the metabolic pathway of linezolid is not fully understood<br>- non-renal clearance accounts ~65%<br>-~30% appears in the urine | <ul style="list-style-type: none"> <li>• Half-life: 4.7 – 5.4 hours</li> <li>• Cmax: 11 – 21 mcg/mL</li> <li>• AUC: 73 – 138 mcg*h/mL</li> <li>• Vd: 40-50 liters</li> </ul>                    |
| tedizolid <sup>11</sup> | - binds to 50S subunit of the bacterial ribosome resulting in inhibition of protein synthesis<br>- bacteriostatic against enterococci, staphylococci, and streptococci  | ~ 91% orally bioavailable<br><br>- not affected by food  | - tedizolid phosphate (prodrug) is ~95% converted to tedizolid; not found to otherwise metabolized<br>- 82% excreted in feces; 18% in urine   | <ul style="list-style-type: none"> <li>• Half-life: 1.2 – 3.5 hours</li> <li>• Cmax: 2 - 3 mcg/mL</li> <li>• AUC: 25 - 29 mcg*h/mL</li> <li>• Vd: 67-80 liters (70-90% protein bond)</li> </ul> |

**Table 4. Use in Specific Populations:**

|                         | FDA Pregnancy Category | Pediatrics   | Geriatrics  |
|-------------------------|------------------------|--|---|
| linezolid <sup>10</sup> | C                      | Safe and effective in children from birth – 12 years for nosocomial pneumonia, ABSSSI, community acquired pneumonia, VRE | No differences in safety or effectiveness observed in patients >65 which comprised 29% of 2046 patients in Phase 3 studies. |
| tedizolid               | C                      | Safety and effectiveness not established for those < 18 years old  | Insufficient number of subjects >65 in Phase 3 studies  |

**Drug Safety:**

Black Boxed Warnings: NA

Contraindications: Patients taking any monoamine oxidase inhibitor (MAOI) or within two weeks of taking an MAOI (linezolid only)

**Table 5. Summary of Warnings and Precautions**

| <b>Warning/Precaution</b>   | <b>linezolid<sup>10</sup></b> | <b>tedizolid<sup>11</sup></b> |
|---|-------------------------------|-------------------------------|
| Myelosuppression: Monitor complete blood counts weekly. Consider discontinuation in patients who develop or have worsening myelosuppression.  | X                             | safety not established        |
| Peripheral and optic neuropathy: Reported primarily in patients treated for longer than 28 days. If patients experience symptoms of visual impairment, prompt ophthalmic evaluation is recommended.   | X                             |                               |
| Serotonin syndrome: Patients taking serotonergic antidepressants should receive ZYVOX only if no other therapies are available. Discontinue serotonergic antidepressants and monitor patients for signs and symptoms of both serotonin syndrome and antidepressant discontinuation. | X                             |                               |
| A mortality imbalance was seen in an investigational study in linezolid treated patients with catheter-related bloodstream infections.  | X                             |                               |
| <i>Clostridium difficile</i> associated diarrhea: Evaluate if diarrhea occurs.  | X                             | X                             |
| Potential interactions producing elevation of blood pressure: monitor blood pressure  | X                             |                               |
| Hypoglycemia: Post-marketing cases of symptomatic hypoglycemia have been reported in patients with diabetes mellitus receiving insulin or oral hypoglycemic agents.   | X                             |                               |

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## Appendix 2: Medline Search Strategy

### 1) Search for published evidence for tedizolid used for pneumonia or VRE indications

Database: Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) <1946 to March Week 2 2015> Search Strategy:

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```
1      tedizolid.mp. (38)
2      Torezolid.mp. (50)
3      TR-701.mp. (18)
4      TR-700.mp. (32)
5      1 or 2 or 3 or 4 (71)
6      gram-positive bacterial infections/ or exp staphylococcal infections/ or exp streptococcal infections/ or
exp pneumonia, staphylococcal/ (122578)
7      exp Vancomycin-Resistant Enterococci/ (23)
8      exp Methicillin-Resistant Staphylococcus aureus/ (7946)
9      6 or 7 or 8 (124584)
10     5 and 9 (28)
11     limit 10 to (English language and humans and (clinical trial, all or meta-analysis or randomized
controlled trial or systematic reviews)) (2)
```

Prokocimer P, Bien P, Deanda C, Pillar CM, Bartizal K. In vitro activity and microbiological efficacy of tedizolid (TR-700) against Gram-positive clinical isolates from a phase 2 study of oral tedizolid phosphate (TR-701) in patients with complicated skin and skin structure infections. *Antimicrobial Agents & Chemotherapy*. 2012; 56(9):4608-13.

#### EXCLUDED – IN VITRO

Prokocimer P, Bien P, Surber J, Mehra P, DeAnda C, Bulitta JB, Corey GR. Phase 2, randomized, double-blind, dose-ranging study evaluating the safety, tolerability, population pharmacokinetics, and efficacy of oral torezolid phosphate in patients with complicated skin and skin structure infections. *Antimicrobial Agents & Chemotherapy*. 2011;55(2):583-92.

#### ABSTRACT

Torezolid (TR-700) is the active moiety of the prodrug torezolid phosphate ([TP] TR-701), a second-generation oxazolidinone with 4- to 16-fold greater potency than linezolid against Gram-positive species including methicillin-resistant *Staphylococcus aureus* (MRSA). A double-blind phase 2 study evaluated three levels (200, 300, or 400 mg) of oral, once-daily TP over 5 to 7 days for complicated skin and skin structure infections (cSSSI). Patients 18 to 75 years old with cSSSI caused by suspected or confirmed Gram-positive pathogens were randomized 1:1:1. Of 188 treated patients, 76.6% had abscesses, 17.6% had extensive cellulitis, and 5.9% had wound infections. *S. aureus*, the most common pathogen, was isolated in 90.3% of patients (139/154) with a baseline pathogen; 80.6% were MRSA. Cure rates in clinically evaluable patients were 98.2% at 200 mg, 94.4% at 300 mg, and 94.4% at 400 mg. Cure rates were consistent across diagnoses, regardless of lesion size or the presence of systemic signs of infection. Clinical cure rates in patients with *S. aureus* isolated at baseline were 96.6% overall and 96.8% for MRSA. TP was safe and well tolerated at all dose levels. No patients discontinued treatment due to an adverse event. Three-stage hierarchical population pharmacokinetic modeling yielded a geometric mean clearance of 8.28 liters/h (between-patient variability, 32.3%), a volume of the central compartment of 71.4 liters (24.0%), and a volume of the peripheral compartment of 27.9 liters (35.7%). Results of this study show a high degree of efficacy at all three dose levels without significant differences in the safety profile and support the continued evaluation of TP for the treatment of cSSSI in phase 3 trials.

#### EXCLUDED – NOT CONTROLLED

## 2) Search for published evidence for tedizolid versus linezolid

Database: Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) <1946 to March Week 2 2015> Search Strategy:

```
-----  
1      tedizolid.mp. (38)  
2      Torezolid.mp. (50)  
3      TR-701.mp. (18)  
4      TR-700.mp. (32)  
5      1 or 2 or 3 or 4 (71)  
6      linezolid.mp. (3414)  
7      5 and 6 (48)  
8      limit 7 to (English language and humans and (clinical trial, all or meta-analysis or randomized controlled  
trial or systematic reviews))(10)
```

### 3 duplicates eliminated - 7 remaining articles)

1-Ong V, Flanagan S, Fang E, Dreskin HJ, Locke JB, Bartizal K, Prokocimer P. Absorption, distribution, metabolism, and excretion of the novel antibacterial prodrug tedizolid phosphate. *Drug Metabolism & Disposition*. 2014; 42(8):1275-84.

2-Flanagan SD, Bien PA, Munoz KA, Minassian SL, Prokocimer PG. Pharmacokinetics of tedizolid following oral administration: single and multiple dose, effect of food, and comparison of two solid forms of the prodrug. *Pharmacotherapy*. 2014; 34(3):240-50, 2014

3-Bien P, De Anda C, Prokocimer P. Comparison of digital planimetry and ruler technique to measure ABSSSI lesion sizes in the ESTABLISH-1 study. *Surgical Infections*. 2014; 15(2):105-10, 2014 Apr.

### EXCLUDED – OUTCOME NOT OF INTEREST

4-Flanagan S, Bartizal K, Minassian SL, Fang E, Prokocimer P. In vitro, in vivo, and clinical studies of tedizolid to assess the potential for peripheral or central monoamine oxidase interactions. *Antimicrobial Agents & Chemotherapy*. 2013; 57(7):3060-6.

5-Prokocimer P, Bien P, Deanda C, Pillar CM, Bartizal K. In vitro activity and microbiological efficacy of tedizolid (TR-700) against Gram-positive clinical isolates from a phase 2 study of oral tedizolid phosphate (TR-701) in patients with complicated skin and skin structure infections. *Antimicrobial Agents & Chemotherapy*. 2012; 56(9):4608-13.

### EXCLUDED – IN VITRO

6-Moran GJ, Fang E, Corey GR, Das AF, De Anda C, Prokocimer P. Tedizolid for 6 days versus linezolid for 10 days for acute bacterial skin and skin-structure infections (ESTABLISH-2): a randomised, double-blind, phase 3, non-inferiority trial. *Lancet Infectious Diseases*. 2014; 14(8):696-705.

7-Prokocimer P; De Anda C; Fang E; Mehra P; Das A. Tedizolid phosphate vs linezolid for treatment of acute bacterial skin and skin structure infections: the ESTABLISH-1 randomized trial. *JAMA*. 2013; 309(6):559-69.

### INCLUDED

Appendix 3: Suggested Prior Authorization Criteria

**Non-preferred Oxazolidinone Antibiotics**

**Goal(s):**

To optimize treatment of infections due to gram-positive organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus faecium* (VRE)

**Length of Authorization:**

6 days

**Requires PA:**

Non-preferred Oxazolidinone Antibiotics

**Covered Alternatives:**

Preferred alternatives listed at [www.orpdl.org](http://www.orpdl.org)

**Approval Criteria**

|   |                               |   |
|---|-------------------------------|---|
| 1. What diagnosis is being treated?   | Record ICD9 code.             |   |
| 2. Does the patient have an active infection with suspected or documented MRSA (e.g. 041.11-041.12, 482.42) or VRE (e.g. V09.8x) or other multi-drug resistant gram-positive cocci (e.g. V09.9x)? | Yes: Go to #3.                | No: Pass to RPH; Deny (medical appropriateness) |
| 3. Does the patient have a documented trial of linezolid, have a contraindication to linezolid, or is the treating organism not susceptible to linezolid?   | Yes: Approve for up to 6 days | No: Pass to RPH; Deny (medical appropriateness) |

P&T / DUR Action: 5/15 (KK)  
Revision(s):  
Initiated: **TBD**