

## PHARMACY COVERAGE GUIDELINE

### SIVEXTRO™ (tedizolid phosphate) oral tablet ZYVOX® (linezolid) oral suspension and tablet

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#### **This Pharmacy Coverage Guideline (PCG):**

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively “Service”) is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider’s judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member’s benefit plan; and
- Is subject to change as new information becomes available.

#### **Scope**

- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

#### **Instructions & Guidance**

- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The “Criteria” section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member’s benefit plan.
- The “Description” section describes the Service.
- The “Definition” section defines certain words, terms or items within the policy and may include tables and charts.
- The “Resources” section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require precertification is available at [www.azblue.com/pharmacy](http://www.azblue.com/pharmacy). You must fully complete the [request form](#) and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to [Pharmacyprecert@azblue.com](mailto:Pharmacyprecert@azblue.com).

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#### **Criteria:**

- **Criteria:** Sivextro (tedizolid) or Zyvox (linezolid) is considered **medically necessary** and will be approved when **ALL** of the following criteria are met:
  1. Prescriber is a physician specializing in the patient’s diagnosis or is in consultation with Infectious Disease, Dermatologist, Podiatrist, or Pulmonologist
  2. Diagnosis is **ONE** of the following:
    - a. **When applicable, to facilitate a hospital discharge**, individual is transitioning from intravenous therapy to oral therapy (the number of days of intravenous use is documented on the request)

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- b. **For Sivextro (tedizolid):** proven or strongly suspected acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible gram-positive bacteria per manufacturer label for individuals 12 years of age or older
  - c. **For Zyvox (linezolid):** proven or strongly suspected clinical infection caused by susceptible gram-positive bacteria per manufacturer label for **ANY** of the following infections:
    - i. Nosocomial pneumonia (from *Streptococcus pneumoniae* or *Staphylococcus aureus*)
    - ii. Community-acquired pneumonia, including concurrent bacteremia (from *Streptococcus pneumoniae* or *Staphylococcus aureus*- *methicillin sensitive* only)
    - iii. Complicated skin and skin structure infections (not decubitus ulcers), including diabetic foot infection without concomitant osteomyelitis (from *Staphylococcus aureus* or *Streptococcus pyogenes* or *Streptococcus agalactiae*)
    - iv. Uncomplicated skin and skin structure infections (from *Staphylococcus aureus*- *methicillin sensitive* only or *Streptococcus pyogenes*)
    - v. Vancomycin-resistant *Enterococcus faecium* infection including concurrent bacteremia
3. Individual has failure, contraindication per FDA label, or intolerance to generic linezolid
  4. Will not be used with or within two weeks of a mono-amine oxidase inhibitor (MAOI)
  5. Will not be used in a patient taking serotonergic agents including serotonin re-uptake inhibitors, tricyclic antidepressants, serotonin 5-HT<sub>1</sub> receptor agonists (triptans), meperidine, bupropion, or buspirone

#### **Approval duration:**

##### **For Sivextro (tedizolid):**

- Maximum duration regardless of route of administration: 6 days total (IV plus oral route)
- IV infusion: MEDICAL BENEFIT ONLY
- No refills will be authorized
- Any request for refill will be reviewed as a new request

##### **For Zyvox (linezolid):**

- Maximum duration regardless of route of administration:
  1. Most infections: 14 days total (IV plus oral route)
  2. Vancomycin resistant *Enterococcus faecium* infection: 28 days total (IV plus oral route)
- IV infusion: MEDICAL BENEFIT ONLY
- No refills will be authorized
- Any request for refill will be reviewed as a new request

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
2. **Off-Label Use of Cancer Medications**

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#### Description:

This Pharmacy Coverage Guideline applies to the out-patient use of Sivextro and Zyvox and should not be utilized for any other purpose.

Zyvox (linezolid) and Sivextro (tedizolid) are oxazolidinone-class antimicrobials used for the treatment of infections caused by susceptible isolates of gram-positive microorganisms. They should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, this information should be considered in selecting or modifying antimicrobial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy. Prescribing either agent in the absence of a proven or strongly suspected bacterial infection or prophylactic indication is unlikely to provide benefit to the individual and increases the risk of the development of drug-resistant bacteria.

Zyvox (linezolid) is indicated in adults and children for the treatment of the following infections caused by susceptible Gram-positive bacteria: Nosocomial pneumonia; Community-acquired pneumonia; Complicated skin and skin structure infections, including diabetic foot infections, without concomitant osteomyelitis; Uncomplicated skin and skin structure infections; and Vancomycin-resistant *Enterococcus faecium* infections.

Sivextro (tedizolid) is indicated in adult and pediatric patients 12 years of age and older for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates of the following Gram-positive microorganisms: *Staphylococcus aureus* (including methicillin-resistant [MRSA] and methicillin-susceptible [MSSA] isolates), *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus anginosus* Group (including *Streptococcus anginosus*, *Streptococcus intermedius*, and *Streptococcus constellatus*), and *Enterococcus faecalis*.

Acute bacterial skin and skin structure infections (ABSSSI) may include cellulitis, erysipelas, wound infections, burns, and major cutaneous abscesses. ABSSSI may present with redness, edema, or induration with lymph node enlargement, purulent drainage or pus within the dermis, and systemic symptoms such as fever.

Common bacterial pathogens causing ABSSSI are *Streptococcus pyogenes* and *Staphylococcus aureus* including methicillin-resistant *Staphylococcus aureus* (MRSA). Less common causes include other *Streptococcus* species, *Enterococcus faecalis*, *Enterococcus faecium*, and Gram-negative bacteria. The incidence of gram positive ABSSSI that requires hospitalization has increased along with an increase in antimicrobial resistant organisms. MRSA has become a common cause of ABSSSI infections and pneumonia in the hospital setting. Infections in individuals who lack the usual risk factors for MRSA have also emerged in the community. As a result, community associated MRSA (CA-MRSA) are now a common cause of ABSSSI. Over reliance with use of Vancomycin has in addition resulted in emergence of resistant strains of certain bacteria such as Vancomycin resistant *Staphylococcus aureus* (VRSA), Vancomycin intermediate *Staphylococcus aureus* (VISA), and Vancomycin resistant *Enterococcus* (VRE).

As a result of rising prevalence of MRSA, empiric therapy for hospitalized individuals with ABSSSI usually includes intravenous use of an antimicrobial with activity against MRSA and an agent that has activity for the other possible pathogens. Out-patients may be managed with a cost effective oral agent.

The approach to treatment ABSSSI and pneumonia and antimicrobial selection is guided by manifestation of infection, severity of clinical presentation, location of infection, and results of culture and sensitivities. Other

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variables to consider in antimicrobial selection include cost, patient risk factors, drug interaction potential, efficacy and safety, monitoring requirements, likely pathogens, and local resistance patterns.

An adequate clinical specimen should be obtained prior to the start of treatment for culture, gram stain, and *in vitro* susceptibility testing. This is an important step for describing the underlying bacterial etiology of the infection. Once these results are known, it may be possible to narrow or change empiric antimicrobial therapy to one that is more cost effective and one that has specific activity for the particular micro-organism present. Depending upon agent chosen, this may allow for transition from intravenous to oral therapy to facilitate discharge to home for hospitalized individuals who are clinically stable to do so.

Numerous antimicrobials are available for treatment of ABSSSI that have activity against gram positive bacteria (including MRSA) as well as the some of the other pathogens involved in the infection. These include Vancomycin (IV, generic), Daptomycin IV (Cubicin), Dalbavacin IV (Dalavance), Oritavancin IV (Orbactiv), Telavancin IV (Vibativ), Ceftaroline IV (Teflaro), Tigecycline IV (Tygacil), Doxycycline (IV and PO, generic), Minocycline (IV and PO), Clindamycin (IV and PO, generic), Trimethoprim-Sulfamethoxazole (IV and PO, generic), Linezolid IV and PO (Zyvox), and Tedizolid IV and PO (Sivextro).

Other antimicrobial agents used for pneumonia can include Amoxicillin + Clavulanate, Cephalosporins, Fluoroquinolone (Levofloxacin, Gemifloxacin, Moxifloxacin, Ofloxacin), Clindamycin, Trimethoprim-sulfamethoxazole, Doxycycline, Minocycline, and Macrolide (Azithromycin, Erythromycin, Clarithromycin).

Both Tedizolid and Linezolid can be administered orally or intravenously. A short 6-day course of Tedizolid has been shown to be statistically non-inferior to a 10-day course of Linezolid for both early and sustained clinical responses in patients with ABSSSIs.

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#### **Definitions:**

##### **Acute bacterial skin and skin structure infection (ABSSSI):**

A bacterial infection of the skin with a lesion size area of at least 75 cm<sup>2</sup> (measured by the area of redness, edema, or induration).

##### **The following infections are defined as ABSSSIs:**

Cellulitis/erysipelas: a diffuse skin infection characterized by spreading areas of redness, edema, and/or induration

Wound infection: an infection characterized by purulent drainage from a wound with surrounding redness, edema, and/or induration

Major cutaneous abscess: an infection characterized by a collection of pus within the dermis or deeper that is accompanied by redness, edema, and/or induration

#### **Spectrum of Activity:**

##### **Sivextro (tedizolid):**

Activity against the following, shown by *in vitro* and clinical infections:

*Enterococcus faecalis*

*Staphylococcus aureus* (includes methicillin resistant (MRSA) & methicillin susceptible (MSSA) isolates)

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*Streptococcus agalactiae*  
*Streptococcus anginosus*  
*Streptococcus intermedius*  
*Streptococcus constellatus*  
*Streptococcus pyogenes*

Zyvox (linezolid):

Activity against the following, shown by *in vitro* and clinical infections:

*Enterococcus faecium* (Vancomycin resistant isolates only)  
*Staphylococcus aureus* (includes MRSA isolates)  
*Streptococcus agalactiae*  
*Streptococcus pneumonia*  
*Streptococcus pyogenes*

Other potential oral anti-microbial therapy for ABSSSI or Pneumonia (dependent on manifestation of infection, severity and location of infection, and results of culture and sensitivities):

Amoxicillin + Clavulanate  
Dicloxacillin  
Cephalosporin  
Fluoroquinolone (Levofloxacin, Gemifloxacin, Moxifloxacin, Ofloxacin)  
Clindamycin  
Trimethoprim-sulfamethoxazole  
Doxycycline  
Minocycline  
Macrolide (Azithromycin, Erythromycin, Clarithromycin)

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### Resources:

Sivextro (tedizolid) product information, revised by Merck Sharp & Dohme Corp. 07-2021. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed September 07, 2021.

Zyvox (linezolid) product information, revised by Pharmacia & Upjohn Company LLC. 04-2021. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed September 07, 2021.

Linezolid powder for suspension product information, revised by West-Ward Pharmaceuticals Corp. 09-2020. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed September 07, 2021.

Linezolid tablet product information, revised by Amneal Pharmaceuticals LLC. 09-2020. Available at at DailyMed <http://dailymed.nlm.nih.gov>. Accessed September 07, 2021.

Spelman D, Baddour LM. Cellulitis and skin abscess in adults: Treatment. In: UpToDate, Lowry FD, Baron EL (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Accessed September 07, 2021.

Lowry FD. Methicillin-resistant *Staphylococcus aureus* (MRSA) in adults: Treatment of skin and soft tissue infections. In: UpToDate, Spelman D, Baron L (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Accessed September 07, 2021.

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Ramirez JA. Overview of community-acquired pneumonia in adults. In: UpToDate, File TM, Bond S (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Accessed September 07, 2021.

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Klompas M. Treatment of hospital-acquired and ventilator-associated pneumonia in adults. In: UpToDate, File TM, Bond S (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Accessed September 07, 2021.

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