BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

**PHARMACY COVERAGE GUIDELINE**

# SIVEXTRO™ (tedizolid phosphate) oral tablet
# ZYVOX® (linezolid) oral suspension and tablet
# Generic Equivalent (if available)

**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 prior authorization is available at 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.

## Criteria:

➢ **Criteria for therapy:** Sivextro (tedizolid) or generic equivalent (if available) 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. Individual's confirmed 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 must be documented on the request)

b. **For Sivextro (tedizolid)**: Proven or strongly suspected acute bacterial skin and skin structure infection (ABSSSI) caused by susceptible gram-positive bacteria as described per manufacturer label for individual who weighs at least 35 kg (see Definitions section)

c. **For Zyvox (linezolid)**: Proven or strongly suspected clinical infection caused by susceptible gram-positive bacteria as described per manufacturer label for **ANY** of the following infections: (see Definitions section)
   i. Nosocomial pneumonia (from *Streptococcus pneumonia* or *Staphylococcus aureus*)
   ii. Community-acquired pneumonia (from *Streptococcus pneumonia*, including concurrent bacteremia 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 documented failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)
   a. **For Sivextro**: Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **generic equivalent if available and generic linezolid**
   b. **For Zyvox**: Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **generic linezolid**

4. **For Sivextro**: Individual does not have neutropenia (neutrophil count is less than 1,000 cells/$mm^3$)

5. **For Zyvox**: Individual does not have catheter-related bloodstream infection or catheter-site infection

6. Individual does not have an infection with any Gram-negative bacteria

7. Will not be used with or within two weeks of a mono-amine oxidase inhibitor (MAOI)

8. Will not be used in a patient taking serotonergic agents including serotonin re-uptake inhibitors, tricyclic antidepressants, serotonin 5-HT1 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, includes any in-patient days)
- 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 includes any in-patient days)

2. Vancomycin resistant *Enterococcus faecium* infection: 28 days total (IV plus oral route includes any in-patient days)

- 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 is 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 (who are at least 26 weeks gestational age and weighing at least 1 kg for intravenous use; and for oral use the individual must weigh 35 kg) 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.

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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 ASSSSI 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 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 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:**

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

**Acute bacterial skin and skin structure infection (ABSSSI):**
A bacterial infection of the skin with a lesion size area of at least 75 $cm^2$ (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, susceptible microorganisms:**
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)
*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, resistance patterns, and results of culture and sensitivities):
Amoxicillin + Clavulanate
Dicloxacillin
Cephalosporin
Fluoroquinolone (Levofloxacin, Gemifloxacin, Moxifloxacin, Ofloxacin)
Clindamycin
Trimethoprim-sulfamethoxazole
Doxycycline

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Minocycline
Macrolide (Azithromycin, Erythromycin, Clarithromycin)

| **Oral antimicrobial therapy for treatment of skin and soft tissue infections due to methicillin-resistant Staphylococcus aureus (MRSA)** | |
|---|---|
| Treatment | Adult dose |
| **Preferred agents** - choice between the preferred oral antibiotic agents is guided by clinical circumstances that includes local antibiotic resistance patterns, allergy history, and use of other medications | |
| Trimethoprim-Sulfamethoxazole | 1 or 2 DS twice daily (with normal renal function) |
| Clindamycin | 450 mg three times daily |
| Doxycycline | 100 mg once daily |
| Minocycline | 200 mg once, then 100 mg twice daily |
| **Alternative agents** - should be reserved for patients who do not respond to or cannot tolerate the preferred agents | |
| Linezolid | 600 mg twice daily |
| Tedizolid | 200 mg once daily |
| Delafloxacin | 450 mg twice daily |
| Omadacycline | 300 mg once daily |

## Resources:

Sivextro (tedizolid) product information, revised by Merck Sharp & Dohme LLC. 04-2025. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed June 27, 2025.

Zyvox (linezolid) product information, revised by Pharmacia & Upjohn Company LLC. 06-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed June 27, 2025.

Linezolid powder for oral suspension product information, revised by Camber Pharmaceuticals, Inc. 07-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 22, 2025.

Linezolid tablet product information, revised by Major Pharmaceuticals. 06-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 22, 2025.

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Klompas M. Treatment of hospital-acquired and ventilator-associated pneumonia in adults. In: UpToDate, File TM, Bogorodskaya M (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through July 2025. Topic last updated June 19, 2024. Accessed August 15, 2025.