

Drug and Biologic Coverage Policy



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Coverage Policy Number 1123

Oxazolidinone Antibiotics

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Related Coverage Resources

[Delafloxacin](#)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Coverage Policy

This coverage policy addresses the use of oral linezolid and tedizolid. The use of intravenous linezolid and tedizolid are not addressed in this coverage policy.

Linezolid (Zyvox®) is considered medically necessary when EITHER of the following are met (1 or 2):

1. Treatment of a known or suspected gram-positive infection caused by **ANY** of the following:
 - a. Methicillin-resistant Staphylococcus infections (for example, MRSA/ORSA, MRSE/ORSE)
 - b. Vancomycin-resistant Enterococcus (VRE)
 - c. Multi-drug resistant Streptococcal infections
 - d. Multi-drug resistant tuberculosis (MDR-TB) infection, as part of a multi-drug regimen
 - e. Nontuberculous atypical mycobacterial infections when prescribed by, or in consultation with, infectious disease specialist
 - f. Infection that is resistant to other antibiotics, but the organism is sensitive to linezolid (if cultures available)
2. For the continuation of linezolid therapy when **ONE** of the following is met:
 - a. The individual is transitioning from intravenous (IV) linezolid or IV vancomycin to oral linezolid therapy

OR

- b. The individual was started on oral linezolid in an inpatient facility and is continuing therapy.

For Individual and Family Plans the following criteria must be met in addition to the criteria above:

- Zyvox (linezolid) tablets are covered when there is documented intolerance to 1 generic formulation of Zyvox tablets.
- Zyvox (linezolid) suspension is covered when there is documented intolerance to 1 generic formulation of Zyvox suspension.

Tedizolid phosphate (Sivextro®) is considered medically necessary when EITHER of the following are met (1 or 2):

1. Treatment of acute bacterial skin and skin structure infections (ABSSSI) and **BOTH** of the following:
 - a. Infection is caused by **ANY** of the following gram-positive microorganisms:
 - Methicillin-Resistant Staphylococcus aureus (MRSA)
 - Selected Streptococcus Species (i.e., Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus anginosus Group)
 - Enterococcus faecalis
 - AND
 - b. Documented failure, contraindication per FDA label, or intolerance to appropriate first-line therapy (for example: ceftriaxone, cefazolin, cephalexin, clindamycin, linezolid, piperacillin-tazobactam, vancomycin)
2. For the continuation therapy of documented Sivextro initiated by IV infusion

Authorization is for a single course of therapy as follows:

- Linezolid for a treatment duration up to 28 days
- Tedizolid phosphate for a treatment duration up to 6 days

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Linezolid and tedizolid phosphate are considered experimental, investigational, or unproven for any other use including the following:

- Treatment of gram-negative infections

Note: Receipt of sample product does not satisfy any criteria requirements for coverage.

FDA Approved Indications

FDA Approved Indication

Zyvox

Zyvox is indicated for the treatment of infections caused by susceptible strains of the designated microorganisms in the specific conditions listed below. Zyvox is not indicated for the treatment of Gram-negative infections. It is critical that specific Gram-negative therapy be initiated immediately if a concomitant Gram-negative pathogen is documented or suspected.

- **Nosocomial pneumonia** caused by Staphylococcus aureus (methicillin-susceptible and -resistant isolates) or Streptococcus pneumoniae.
- **Community-acquired pneumonia** caused by Streptococcus pneumoniae, including cases with concurrent bacteremia, or Staphylococcus aureus (methicillin-susceptible isolates only).
- **Complicated skin and skin structure infections, including diabetic foot infections, without concomitant osteomyelitis**, caused by Staphylococcus aureus (methicillin-susceptible and -resistant

isolates), *Streptococcus pyogenes*, or *Streptococcus agalactiae*. Zyvox has not been studied in the treatment of decubitus ulcers.

- **Uncomplicated skin and skin structure infections** caused by *Staphylococcus aureus* (methicillin-susceptible isolates only) or *Streptococcus pyogenes*.
- **Vancomycin-resistant *Enterococcus faecium* infections**, including cases with concurrent bacteremia.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Zyvox and other antibacterial drugs, Zyvox 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, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

The safety and efficacy of Zyvox formulations given for longer than 28 days have not been evaluated in controlled clinical trials.

Sivextro

Sivextro is an oxazolidinone-class antibacterial indicated 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*.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Sivextro and other antibacterial drugs, Sivextro should be used only to treat ABSSSI that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Recommended Dosing

FDA Recommended Dosing

Zyvox

Dosage Guidelines for Zyvox

Infection*	Dosage, Route and Frequency of Administration		Recommended Duration of Treatment (consecutive days)
	Pediatric Patients [†] (Birth through 11 Years of Age)	Adults and Adolescents (12 Years and Older)	
Nosocomial pneumonia	10 mg/kg intravenously or oral [†] every 8 hours	600 mg intravenously or oral [†] every 12 hours	10 to 14
Community-acquired pneumonia, including concurrent bacteremia			
Complicate skin and skin structure infections			
Vancomycin-resistant <i>Enterococcus faecium</i> infections, including concurrent bacteremia	10 mg/kg intravenously or oral [†] every 8 hours	600 mg intravenously or oral [†] every 12 hours	14 to 28
Uncomplicated skin and skin structure infections	Less than 5 yrs: 10 mg/kg oral [†] every 8 hours 5-11 yrs: 10 mg/kg oral [†] every 12 hours	Adults: 400 mg oral [†] every 12 hours Adolescents: 600 mg oral [†] every 12 hours	10 to 14

* Due to the designated pathogens

[†] Neonates less than 7 days: Most pre-term neonates less than 7 days of age (gestational age less than 34 weeks) have lower systemic linezolid clearance values and larger AUC values than many full-term neonates and older infants. These neonates should be initiated with a dosing regimen of 10 mg/kg every 12 hours. Consideration may be given to the use of 10

mg/kg every 8 hours regimen in neonates with a sub-optimal clinical response. All neonatal patients should receive 10 mg/kg every 8 hours by 7 days of life.

† Oral dosing using either Zyvox Tablets or Zyvox for Oral Suspension.

No dose adjustment is necessary when switching from intravenous to oral administration.

Sivextro

The recommended dosage of Sivextro is 200 mg administered once daily for six (6) days either orally (with or without food) or as an intravenous (IV) infusion in patients 18 years of age or older.

No dose adjustment is necessary when changing from intravenous to oral Sivextro.

Drug Availability

Zyvox

Supplied as a 600 mg tablet of linezolid or as a powder for oral suspension that when reconstituted as directed, contains a total of 150 mL of a suspension at a concentration of 100 mg of linezolid per each 5 mL.

Sivextro

Supplied as a 200 mg tablet of tedizolid phosphate.

General Background

OVERVIEW

Linezolid (Zyvox) and Sivextro are synthetic oxazolidinone antimicrobial agents.^{1,2} Both agents have clinical utility in the treatment of infections caused by aerobic Gram-positive bacteria. Cross-resistance between linezolid or Sivextro and other classes of antibiotics is unlikely because the mechanism of action for both these agents differs from that of other antibacterial agents.

Linezolid is indicated in adults and children for the treatment of the following infections caused by susceptible strains of the designated microorganisms:¹

- Vancomycin-resistant *Enterococcus faecium* (VRE) infections, including cases with concurrent bacteremia;
- Nosocomial pneumonia caused by *Staphylococcus aureus* (methicillin-susceptible [MSSA] and methicillin-resistant strains [MRSA]), or *Streptococcus pneumoniae*;
- Complicated skin and skin structure infections (cSSTIs), including diabetic foot infections, without concomitant osteomyelitis caused by *S. aureus* (MSSA and MRSA), *Streptococcus pyogenes*, or *Streptococcus agalactiae*. Zyvox has not been studied in the treatment of decubitus ulcers;
- Uncomplicated skin and skin structure infections (SSTIs) caused by *S. aureus* (MSSA only) or *S. pyogenes*; and
- Community-acquired pneumonia (CAP) caused by *S. pneumoniae*, including cases with concurrent bacteremia, or *S. aureus* (MSSA only).

Sivextro is indicated for the treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults that are caused by susceptible isolates of the following Gram-positive microorganisms: *S. aureus* (MRSA and MSSA), *S. pyogenes*, *S. agalactiae*, *Streptococcus anginosus* Group (including *S. anginosus*, *Streptococcus intermedius*, and *Streptococcus constellatus*), and *Enterococcus faecalis*.²

Although linezolid and Sivextro are indicated for susceptible strains of MSSA and drug-resistant strains of *S. pneumoniae* in some situations, it is not the optimal drug or drug of first-choice for these microorganisms.³⁻⁴ Other antibiotics may be used. In efforts to reduce the development of drug-resistant bacteria and maintain effectiveness of linezolid and Sivextro, both antibiotics should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria.^{1,2} When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Guidelines

MRSA

The 2011 Infectious Diseases Society of America (IDSA) guidelines for the treatment of MRSA infections recognize linezolid as a treatment option for other infections including infections of the central nervous system (CNS [e.g., meningitis, brain abscess]), osteomyelitis, and septic arthritis.⁵

Diabetic Foot Infections

A clinical practice guideline for the diagnosis and treatment of diabetic foot infections (IDSA 2012) notes that diabetic foot infections of moderate severity may be treated with oral or initial parenteral therapy, while severe infections should be treated with parenteral therapy.⁶ Linezolid, Cubicin® (daptomycin injection), and intravenous (IV) vancomycin are listed as therapy options for infections caused by MRSA (linezolid is the only oral therapy in this grouping).

Skin and Soft Tissue Infections (SSTIs)

According to the IDSA guidelines (2014) for the diagnosis and management of SSTIs, for mild nonpurulent (i.e., necrotizing infection, cellulitis, erysipelas) SSTI, oral antibiotics such as penicillin VK, cephalosporin, dicloxacillin, or clindamycin can be used.⁷ For moderate nonpurulent SSTI, IV antibiotics such as penicillin, ceftriaxone, ceftazolin, or clindamycin are recommended. For moderate purulent SSTIs, empiric treatment can be started with trimethoprim/sulfamethoxazole (TMP/SMX) or doxycycline. For MRSA infections, TMP/SMX is the recommended therapy. Cephalexin or dicloxacillin are usually effective for MSSA infections. For severe purulent SSTI, empiric therapy with IV vancomycin, Cubicin, linezolid, Vibativ® (telavancin powder for injection), or Teflaro® (ceftaroline powder for injection) are recommended. All of these agents are active against MRSA strains. For severe purulent SSTI caused by MSSA, therapy can be switched to nafcillin, ceftazolin, or clindamycin.

Pneumonia

Guidelines from the American Thoracic Society (ATS) and IDSA (2016) recommend that MRSA hospital-acquired pneumonia (HAP) or ventilator-associated pneumonia (VAP) be treated with either vancomycin or linezolid rather than other antibiotics or other antibiotic combinations.⁴ The choice between vancomycin and linezolid may be guided by patient-specific factors such as blood cell counts, concurrent prescriptions for serotonin-reuptake inhibitors, renal function, and cost. The available evidence indicates that vancomycin and linezolid are roughly similar and no alternative agent or regimen is clearly superior to these two products. Guidelines from the IDSA/ATS (2007) for community-acquired pneumonia (CAP) recommend vancomycin or linezolid for the treatment of community-acquired MRSA.³ In addition, the Pediatric Infectious Disease Society and the IDSA guidelines (2011) for the treatment of CAP in infants and children > 3 months of age recommend linezolid as an alternative to vancomycin for treatment of MRSA, and as an alternative to ceftriaxone for the treatment of *S. pneumoniae* resistant to penicillin.⁸

Infective Endocarditis

Treatment guidelines, from the American Heart Association and endorsed by the IDSA (2015), recommend linezolid as a treatment option for patients with infective endocarditis caused by *Enterococcus* species that is resistant to penicillin, aminoglycosides, and vancomycin.⁹

Coding/Billing Information

Note: Zyvox and Sivextro are typically covered under pharmacy benefit plans. Certain prescription drugs require an authorization for coverage to ensure that appropriate treatment regimens are followed. Medical drug coding and diagnosis codes, however, are generally not required for pharmacy claims submissions, therefore, this section is not in use.

References

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