PRIOR AUTHORIZATION POLICY

POLICY: Antibiotics – Linezolid (Zyvox), Sivextro Prior Authorization Policy
- Linezolid tablets, oral suspension (Zyvox® – Pfizer, generics)
- Sivextro™ (tedizolid phosphate tablets – Cubist Pharmaceuticals)

REVIEW DATE: 10/14/2020

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 of 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]
- **Community-acquired pneumonia** (CAP), caused by *S. pneumoniae*, including cases with concurrent bacteremia, or *S. aureus* (MSSA only);
- **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;
- **Nosocomial pneumonia**, caused by *Staphylococcus aureus* (methicillin-susceptible [MSSA] and methicillin-resistant strains [MRSA]), or *Streptococcus pneumoniae*;
- **Uncomplicated skin and skin structure infections** (SSTIs), caused by *S. aureus* (MSSA only) or *S. pyogenes*;
- **Vancomycin-resistant *Enterococcus faecium* (VRE) infections**, including cases with concurrent bacteremia.

Sivextro is indicated for the treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults and pediatric patients ≥ 12 years of age 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

Diabetic Foot Infections

A clinical practice guideline for the diagnosis and treatment of diabetic foot infections (Infectious Diseases Society of America [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).

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]

MRSA

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

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 (2019) for 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]

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, cefazolin, 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, cefazolin, or clindamycin.

POLICY STATEMENT
Prior authorization is recommended for prescription benefit coverage of linezolid and Sivextro. All approvals are provided for the duration noted below. In cases where approval is in months, 1 month is equal to 30 days.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

A. Coverage of linezolid is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Vancomycin-Resistant *Enterococcus* (VRE) Species Infection, Treatment**. Approve for 1 month.

2. **Methicillin-Resistant *Staphylococcus* Species Infection, Treatment**. Approve for 1 month.

Other Uses with Supportive Evidence

3. **Continuation of Linezolid Therapy.** Approve for 1 month in patients who meet ONE of the following criteria (a or b):
   a) Patient is transitioning from intravenous (IV) linezolid or IV vancomycin to oral linezolid therapy; OR
   b) Patient was started on oral linezolid in an inpatient facility and is continuing therapy.

4. **Treatment of an Infection that is Resistant to Other Antibiotics, but the Organism is Sensitive to Linezolid.** Approve for 1 month.

5. **There is Insufficient Information Available to Make a Determination Regarding Coverage and the Prescriber or Representative Cannot be Contacted.** Approve for up to 2 weeks of therapy.

   To avoid delays or disruption in therapy for the patient, if there is insufficient information available to make a determination regarding coverage and the prescriber or representative of the prescriber cannot be contacted, approve linezolid for up to 2 weeks.

B. Coverage of Sivextro is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Acute Bacterial Skin and Skin Structure Infections (ABSSSI) Caused by Methicillin-Resistant *Staphylococcus aureus* (MRSA), Selected *Streptococcus* Species (i.e., *Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus anginosus* Group) and *Enterococcus faecalis*.** Approve for up to 6 days of therapy.

Other Uses with Supportive Evidence

2. **Continuation of Sivextro Therapy in the Outpatient Setting.** Approve for up to 6 days of therapy in patients transitioning from Sivextro IV therapy to oral therapy.

3. **There is Insufficient Information Available to Make a Determination Regarding Coverage and the Prescriber or Representative Cannot be Contacted.** Approve for up to 6 days of therapy.

   To avoid delays or disruption in therapy for the patient, if there is insufficient information available to make a determination regarding coverage and the prescriber or representative of the prescriber cannot be contacted, approve Sivextro. Since the available data for Sivextro only supports up to 6 days of therapy for the ABSSSI indication, we are limiting approval to this duration.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of linezolid and Sivextro is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria for both linezolid and Sivextro. Criteria will be updated as new published data are available.

REFERENCES

1. Zyvox® injection, tablets, and for oral suspension [prescribing information]. New York, NY: Pfizer; August 2020.
2. Sivextro™ tablets [prescribing information]. Lexington, MA: Cubist Pharmaceuticals; June 2020.
3. Metlay JP, Waterer GW, Long AC, et al. Diagnosis and treatment of adults with community-acquired pneumonia. An official practice guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med*. 2019;200:e45-e67.
4. Kalil AC, Metersky ML, Klompas M, et al. Management of adults with hospital-aquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis*. 2016;63:e61–e111.
5. 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;52:1-38.
6. Lipsky BA, Berendt AR, Corina PB, et al. 2012 Infectious Diseases Society of America clinical practice guidelines for the diagnosis and treatment of diabetic foot infections. *CID*. 2012;54:e132-e172.
7. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2014;59:e10-e52.
8. Bradley JS, Byington CL, Shah SS, et al. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. *Clin Infect Dis*. 2011;53(7):e25-76.
9. Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis in adults: Diagnosis, antimicrobial therapy, and management of complications: A scientific statement for healthcare professionals from the committee on rheumatic fever, endocarditis, and rheumatic fever, Council on cardiovascular disease in the young, and the Councils on clinical cardiology, stroke, and cardiovascular surgery, and anesthesia, American Heart Association: Endorsed by the Infectious Diseases Society of America. *Circulation*. 2015;132:1435-1486.