Clinical Policy: Linezolid (Zyvox)

Reference Number: LA.PMN.27
Effective Date:
Last Review Date: 03.21 **Coding Implications**
Line of Business: Medicaid **Revision Log**

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Linezolid (Zyvox®) is an oxazolidinone-class antibacterial agent.

FDA Approved Indication(s)

Zyvox is indicated in adults and children for the treatment of the following infections caused by susceptible gram-positive bacteria:

- **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**

Limitation(s) of use:

- **Zyvox is not indicated for the treatment of Gram-negative infections.**
- **The safety and efficacy of Zyvox formulations given for longer than 28 days have not been evaluated in controlled clinical trials.**

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Zyvox formulations and other antibacterial drugs, Zyvox should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

Policy/Criteria

Prior authorization is required. Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections that Zyvox is medically necessary when the following criteria are met:

I. Initial Approval Criteria

A. All FDA-Approved Indications (must meet all):

1. **Diagnosis is an FDA-approved indication;**
2. **Member meets one of the following (a or b):**
   a. **Request is for continuation of therapy initiated in an acute care hospital from which member was discharged;**
   b. **Both of the following (i and ii):**
      i. **Culture and sensitivity (C&S) report for the current infection shows isolated pathogen is a gram-positive bacteria susceptible to linezolid, unless provider submits documentation that obtaining a C&S report is not feasible;**
      ii. **Member meets one of the following (a, b, or c):**
         a) **Failure of ≥ 2 formulary antibiotics to which the isolated pathogen is susceptible (if available) per C&S report, unless all are contraindicated or clinically significant adverse effects are experienced;**
         b) **C&S report shows resistance or lack of susceptibility of the isolated pathogen to all formulary antibiotics FDA-approved for member's diagnosis;**
         c) **If provider documents that obtaining a C&S report is not feasible: Failure of ≥ 2 formulary antibiotics indicated for member's diagnosis (if available), unless all are contraindicated or clinically significant adverse effects are experienced;**
3. **Dose does not exceed 1,200 mg (2 vials) per day.**

Approval duration: Duration of request or up to 28 days of total treatment, whichever is less

B. Other diagnoses/indications

1. **Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized LA.PMN.53 for Medicaid.**

II. Continued Therapy

A. All FDA-Approved Indications (must meet all):

1. **Member meets one of the following (a or b):**
   a. **Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;**
   b. **Request is for continuation of therapy initiated in an acute care hospital from which member was discharged;**
2. **Member is responding positively to therapy;**
3. **Member has not received ≥ 28 days of therapy for current infection;**
4. **If request is for a dose increase, new dose does not exceed 1,200 mg (2 vials) per day.**

Approval duration: Up to 28 days of total treatment

B. Other diagnoses/indications (must meet 1 or 2):
1. **Currently receiving medication via Louisiana Healthcare Connections benefit and documentation supports positive response to therapy.**
Approval duration: Duration of request or 28 days (whichever is less); or
2. **Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.**

III. Diagnoses/Indications for which coverage is NOT authorized:
A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy –LA.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information
Appendix A: Abbreviation/Acronym Key
C&S: culture and sensitivity
CDC: Centers for Disease Control and Prevention
FDA: Food and Drug Administration
MDR-TB: multi-drug resistant tuberculosis
XDR-TB: extensively drug resistant tuberculosis

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
pretomanid	200 mg PO QD for 26 weeks.	200 mg/day
Sirturo® (bedaquiline)	400 mg PO QD for the first 2 weeks, followed by 200 mg PO three times per week for remaining 24 weeks.	400 mg/day
Therapeutic alternatives include formulary antibiotics that are indicated for member's diagnosis and have sufficient activity against the offending pathogen at the site of the infection.		

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
- **Contraindication(s):**
  - **Known hypersensitivity to linezolid or any of the other product components**
  - **Patients taking any monoamine oxidase inhibitors (MAOI) within two weeks of taking an MAOI**
- **Boxed warnings(s): none reported**

Appendix D: General Information

For MDR-TB or XDR-TB with pretomanid:

- **Centers for Disease Control and Prevention (CDC) Centers of Excellence for TB: https://www.cdc.gov/tb/education/tb_coe/default.htm**
- **Pretomanid should only be used in combination with Sirturo and linezolid.**
- **Dosing of the combination regimen of pretomanid, Sirturo, and linezolid can be extended beyond 26 weeks if necessary, to a maximum of 9 months, in patients with delayed culture conversion.**
  - **Delayed culture conversion: two consecutive negative sputum cultures following an initial positive culture.**
- **Laboratory confirmation of multi-drug resistant TB must show TB with an isolate showing genotypic or phenotypic resistance to isoniazid and rifampin.**
- **Laboratory confirmation of extensively drug resistant TB must show TB with an isolate showing genotypic or phenotypic resistance to isoniazid, rifampin, fluoroquinolones, as well as second-line injectable agents such as aminoglycosides or capreomycin.**
- **Linezolid starting dose of 1,200 mg daily for 26 weeks may be managed as follows:**
  - **Adjusted to 600 mg daily and further reduced to 300 mg daily as necessary for adverse reactions of myelosuppression, peripheral neuropathy, and optic neuropathy.**
  - **Doses of the regiment missed for safety reasons can be made up at the end of treatment; does of linezolid alone missed due to adverse reactions should not be made up.**

V. Dosage and Administration

Indication	Dosing Regimen			Maximum Dose
	Pediatrics (birth – age 11 years)	Adults and Adolescents (age ≥ 12 years)	Duration (consecutive days)	
Nosocomial pneumonia	10 mg/kg IV every 8 hours	600 mg IV every 12 hours	10 to 14	Adults and adolescents age ≥ 12 years: 1,200 mg/day Age 1 – 11 years: 10 mg/kg/dose IV every 8 hours (max: 600 mg/dose) Infants and neonates: 10 mg/kg/dose IV every 8 hours
Community-acquired pneumonia, including concurrent bacteremia				
Complicated skin and skin structure infections				
Vancomycin-resistant *Enterococcus faecium* infections, including concurrent bacteremia	10 mg/kg IV every 8 hours	600 mg IV every 12 hours	14 to 28	

VI. Product Availability

- Injection: 200 mg/100 mL and 600mg /300 mL

VII. References

1. Zyvox Prescribing Information. New York, NY; Pfizer Inc.; October 2020. Available at: http://labeling.pfizer.com/showlabeling.aspx?id=649 Accessed November 24, 2020.
2. Linezolid Drug Monograph. Clinical Pharmacology. Accessed November 2020. http://www.clinicalpharmacology-ip.com.
3. 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; Jul 15;59(2):147-59.
4. Ament PW, Jamshed, N., Horne JP. Linezolid: its role in the treatment of gram-positive, drug-resistant bacterial infections. Am Fam Physician. 2002 Feb 15;65(4):663-671. www.aafp.org/afp/20020215/663.html.
5. C Liu, et al. Management of patients with infections caused by methicillin-resistant Staphylococcus aureus: clinical practice guidelines by the Infectious Diseases Society of America (IDSA). Clinical Infectious Diseases; 2011;52:1-38.
6. Pretomanid Prescribing Information. Hyderabad, India: Mylan; August 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212862s000lbl.pdf. Accessed September 6, 2019.

7. **FDA Briefing Document for Pretomanid tablet, 200mg. Meeting of the Antimicrobial Drugs Advisory Committee (AMDAC): New York, NY: June 6, 2019. Available at: https://www.fda.gov/media/127592/download. Accessed September 6, 2019.**
8. **Pretomanid: Sponsor Briefing Document Antimicrobial Drugs Advisory Committee. New York, NY: June 6, 2019. Available at: https://www.fda.gov/media/127593/download. Accessed September 6, 2019.**
9. **Metlay J, Waterer G, Long A, et al. Diagnosis and treatment of adults with community-acquired pneumonia: An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of American. American Thoracic Society Documents. Oct 2019; 200(7):e45-67**

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J2020	Injection, linezolid, 200 mg

Reviews, Revisions, and Approvals	Date
Converted corporate to local policy.	03.21

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions,

exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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