

Clinical Policy: Linezolid (Zyvox)

Reference Number: CP.PMN.27

Effective Date: 09.01.06

Last Review Date: 02.19

Line of Business: HIM*, Medicaid

[Coding Implications](#)

[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.

**For Health Insurance Marketplace (HIM), if request is through the pharmacy benefit, the intravenous formulation is non-formulary and cannot be approved using these criteria; refer to the formulary exception policy, HIM.PA.103.*

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

Policy/Criteria

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 health plans affiliated with Centene Corporation[®] 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. Prescribed by or in consultation with an infectious disease specialist;
3. 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;
4. Dose does not exceed 1,200 mg (2 tablets, 2 vials, or 60 mL suspension) per day.

Approval duration:

Medicaid – Duration of request or up to 28 days of total treatment, whichever is less

HIM – Duration of request or up to 28 days of total treatment, whichever is less, for oral formulations (*refer to HIM.PA.103 for intravenous formulation*)

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace and CP.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 Centene 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 tablets, 2 vials, or 60 mL suspension) per day.

Approval duration:

Medicaid – Up to 28 days of total treatment

HIM – Up to 28 days of total treatment for oral formulations (*refer to HIM.PA.103 for intravenous formulation*)

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene 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 for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace and CP.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 policies – HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

C&S: culture and sensitivity

FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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

V. Dosage and Administration

Indication	Dosing Regimen			Maximum Dose
	Pediatrics (birth – age 11 years)	Adults and Adolescents (age ≥ 12 years)	Duration (consecutive days)	Adults and adolescents age ≥ 12 years: 1,200 mg/day
Nosocomial pneumonia	10 mg/kg IV or PO every 8 hours	600 mg IV or PO every 12 hours	10 to 14	Age 1 – 11 years: 10 mg/kg/dose PO or IV every 8 hours (max: 600 mg/dose)
Community-acquired pneumonia, including concurrent bacteremia				
Complicated skin and skin structure infections				
Vancomycin-resistant <i>Enterococcus faecium</i> infections, including concurrent bacteremia	10 mg/kg IV or PO every 8 hours	600 mg IV or PO every 12 hours	14 to 28	Infants and neonates: 10 mg/kg/dose PO or IV every 8 hours
Uncomplicated skin and skin structure infections	Age < 5 years: 10 mg/kg PO every 8 hours Age 5 – 11 years: 10 mg/kg PO every 12 hours	Adults: 400 mg PO every 12 hours Adolescents: 600 mg PO every 12 hours	10 to 14	

VI. Product Availability

- Injection: 200 mg, 400 mg, 600 mg
- Tablets: 600 mg
- Oral suspension: 100 mg/5 mL

VII. References

1. Zyvox Prescribing Information. New York, NY; Pfizer Inc.; July 2018. Available at: <http://www.zyvox.com/>. Accessed October 30, 2018.
2. Linezolid Drug Monograph. Clinical Pharmacology. Accessed October 2018. <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.

- 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.

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	P&T Approval Date
Removed requirement related to documentation of an FDA approved indication. Added prescriber specialty. Added that culture and sensitivity report must show pathogen susceptibility to linezolid and be dated within the last 7 days. Added requirement related to trial and failure of formulary antibiotics to which pathogen is susceptible, unless contraindicated to such therapies, or culture and sensitivity report shows resistance of pathogen to formulary antibiotics. Updated continuation criteria. Updated references. Changed guideline to new format.	11.16	11.16
Clinical changes made to criteria: Modified criteria to allow for cases in which obtaining C&S report is not feasible per documentation from the provider Removed language specifying “Isolated pathogen is VRE” since VRE is gram-positive and policy covers gram positive bacteria Added max dose requirement in initial approval criteria Non-clinical changes made: Converted to new template Updated policy name to reflect linezolid tablets since the oral suspension is on the formulary and does not require a PA Updated references	01.17	
2Q 2018 annual review: no significant changes; safety updated per safety guidance endorsed by Centene Medical Affairs; references reviewed and updated.	03.06.18	05.18
1Q 2019 annual review: added criterion line for diagnosis to be an FDA-approved indication; removed 7 day requirement for C&S report and replaced it with requirement that C&S report is for the current infection; clarified that pathogen susceptibility to antibiotics be demonstrated via C&S report; added ‘lack of susceptibility’ as an alternative to demonstrating resistance on C&S; removed criterion allowing member to meet criteria if formulary antibiotics are not	10.30.18	02.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
indicated for member’s diagnosis, since this is incorporated into other existing criteria already; added criterion to allow member to continue treatment if it was started in an acute care hospital and member was discharged; references reviewed and updated.		

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. The Health Plan 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. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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 Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. 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. The Health Plan 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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy; HIM.PA.103.

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