

**Clinical Policy: Lefamulin (Xenleta)**

Reference Number: CP.PMN.219

Effective Date: 03.01.20

Last Review Date: 02.21

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

**Description**

Lefamulin (Xenleta<sup>™</sup>) is a systemic pleuromutilin antibacterial drug.

**FDA Approved Indication(s)**

Xenleta is indicated for the treatment of adults with community-acquired bacterial pneumonia (CABP) caused by the following susceptible microorganisms: *Streptococcus pneumoniae*, *Staphylococcus aureus* (methicillin-susceptible isolates), *Haemophilus influenzae*, *Legionella pneumophila*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae*.

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

**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<sup>®</sup> that Xenleta is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria****A. Community-Acquired Bacterial Pneumonia (must meet all):**

1. Diagnosis of CABP;
2. Age  $\geq$  18 years;
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 susceptible to Xenleta, 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  $\geq$  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  $\geq 2$  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 PO (2 tablets) or 300 mg IV (2 vials) per day.

**Approval duration: Duration of request or up to 7 days of total treatment, whichever is less**

**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): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid

**II. Continued Therapy**

**A. Community-Acquired Bacterial Pneumonia (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  $\geq 7$  days of therapy for current infection;
4. If request is for a dose increase, new dose does not exceed 1,200 mg PO (2 tablets) or 300 mg IV (2 vials) per day.

**Approval duration: Up to 7 days of total treatment**

**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 7 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): CP.CPA.09 for commercial, 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 – CP.CPA.09 for commercial, 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*

FDA: Food and Drug Administration  
CABP: community-acquired bacterial pneumonia  
C&S: culture and sensitivity

*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<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): known hypersensitivity to lefamulin, pleuromutilin class drugs, or any of the components of Xenleta; concomitant use of Xenleta tablets with CYP3A substrates that prolong the QT interval
- Boxed warning(s): none reported

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
CABP	PO: 600 mg (1 tablet) PO q12h for 5 days.  IV: 150 mg (1 vial) q12h IV over 60 minutes (with the option to switch to Xenleta 600 mg tablets PO q12h to complete the treatment course) for 5 to 7 days.	PO: 1,200 mg/day IV: 300 mg/day

**VI. Product Availability**

- Tablets: 600 mg
- Vial for injection: 150 mg

**VII. References**

1. Xenleta Prescribing Information. Nabriva Therapeutics US, Inc; October 2019. Available at: <http://www.xenleta.com/>. Accessed November 30, 2020.
2. Mandell L, Wunderink R, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007 Mar 1;44 Suppl 2:S27-72. Available at <https://www.ncbi.nlm.nih.gov/pubmed/17278083>. Accessed September 12, 2019.
3. File T, Goldberg L, Das A, et al. Efficacy and Safety of IV-to-Oral Lefamulin, a Pleuromutilin Antibiotic, for Treatment of Community-Acquired Bacterial Pneumonia: The

Phase 3 LEAP 1 Trial. Clin Infect Dis. 2019 Feb 4. doi: 10.1093/cid/ciz090. [Epub ahead of print]

4. Alexander E, Goldberg L, Das A, et al. LB6. Oral Lefamulin Is Safe and Effective in the Treatment of Adults With Community-Acquired Bacterial Pneumonia (CABP): Results of Lefamulin Evaluation Against Pneumonia (LEAP 2) Study. Open Forum Infect Dis. 2018;5(Suppl 1):S761. Published 2018 Nov 26. doi:10.1093/ofid/ofy229.2180. Available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6253245/>. Accessed September 12, 2019.
5. Metley JP, Waterer GW, Long AC, 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 America. Am J Respir Crit Care Med. 2019 Oct 1;200(7):e45-e67.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	10.08.19	02.20
1Q 2021 annual review: no significant changes; references reviewed and updated.	11.30.20	02.21

**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. 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.

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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.

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