# Clinical Policy: Lefamulin (Xenleta)

Reference Number: CP.PMN.219
Effective Date: 03.01.20
Last Review Date: 08.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Coding Implications
Revision Log

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

## Description

Lefamulin (Xenleta™) 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 *Chlamydophila 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. 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.

## 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 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 ≥ 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):*
      **For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395*

a) Failure of ≥ 2 formulary antibiotics to which the isolated pathogen is susceptible (if available) per C&S report, unless clinically significant adverse effects are experienced or all are contraindicated;
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 clinically significant adverse effects are experienced or all are contraindicated;

4. Dose does not exceed one of the following (a or b):
   a. 1,200 mg PO (2 tablets);
   b. 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** (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, 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, b, or c):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
   c. 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 ≥ 7 days of therapy for current infection;

4. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. 1,200 mg PO (2 tablets);
   b. 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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, 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.PA.154 for health insurance marketplace/ICHRA, 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® (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 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.<br><br>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<br>IV: 300 mg/day |

## VI. Product Availability

- Tablet: 600 mg
- Single-dose vial for injection: 150 mg

## VII. References

1. Xenleta Prescribing Information. Nabriva Therapeutics US, Inc; June 2021. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=101db63d-2fe2-48df-8506-1382d6dcd4a3. Accessed April 8, 2026.
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.

6. Jones BE, Ramirez JA, Oren E, et al.; American Thoracic Society Assembly on Pulmonary Infections and Tuberculosis. Diagnosis and Management of Community-acquired Pneumonia: An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med. 2026 Jan 1;212(1):24-44. doi: 10.1164/rccm.202507-1692ST.

**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 |
|---|---|
| J0691 | Injection, lefamulin, 1 mg |
| C9399 | Unclassified drugs or biologicals |
| J8499 | Prescription drug, oral, non chemotherapeutic, nos |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| 1Q 2023 annual review: no significant changes; references reviewed and updated. | 10.04.22 | 02.23 |
| 3Q 2023 annual review: no significant changes; added HCPCS codes C9399 and J8499; references reviewed and updated. | 04.12.23 | 08.23 |
| 3Q 2024 annual review: no significant changes; references reviewed and updated. | 05.09.24 | 08.24 |
| 3Q 2025 annual review: no significant changes; references reviewed and updated.<br>Added step therapy bypass for IL HIM per IL HB 5395. | 06.26.25 | 08.25 |
| 3Q 2026 annual review: no significant changes; references reviewed and updated.<br>Added ICHRA line of business. | 04.08.26 | 08.26 |

**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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**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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