Clinical Policy: Lefamulin (Xenleta)

Reference Number: ERX.NPA.134
Effective Date: 03.01.20
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

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.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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):
         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 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 ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 a health plan affiliated with Envolve Pharmacy Solutions 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 ≥ 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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 7 days (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 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 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.	PO: 1,200 mg/day IV: 300 mg/day

Indication	Dosing Regimen	Maximum Dose
	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.	

VI. Product Availability

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

VII. References

1. Xenleta Prescribing Information. Nabriva Therapeutics US, Inc; March 2021. Available at: http://www.xenleta.com/. Accessed September 30, 2021.
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
1Q 2022 annual review: no significant changes; references reviewed and updated.	09.30.21	02.22

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.