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5.01.055

Section:	Prescription Drugs	**Effective Date:**	July 1, 2024
Subsection:	Anti-infective Agents	**Original Policy Date:**	January 17, 2020
Subject:	Xenleta	**Page:**	1 of 4

Last Review Date: June 13, 2024

Xenleta

Description

Xenleta (lefamulin)

Background
Xenleta (lefamulin) is a systemic pleuromutilin antibacterial. It inhibits bacterial protein synthesis through interactions with the A- and P-sites of the peptidyl transferase center (PTC) in domain V of the 23s rRNA of the 50S subunit. The binding pocket of the bacterial ribosome closes around the mutilin core for an induced fit that prevents correct positioning of tRNA. Xenleta is bactericidal against *S. pneumoniae*, *H. influenzae*, and *M. pneumoniae*, and bacteriostatic against *S. aureus* and *S. pyogenes* at clinically relevant concentrations (1).

Regulatory Status
FDA-approved indications: 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 influenza*, *Legionella pneumophila*, *Mycoplasma pneumoniae*, and *Chlamydophila pneumoniae* (1).

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 susceptible bacteria (1).

Xenleta has the potential to prolong the QT interval of the electrocardiogram (ECG) in some patients. If use with Xenleta cannot be avoided in specific populations predisposed to QT

prolongation or those receiving another drug that prolongs the QT interval, ECG monitoring is recommended during treatment (1).

Xenleta may cause fetal harm when administered to pregnant women. Pregnancy status should be verified in females of reproductive potential prior to initiating Xenleta. Females of reproductive potential should be advised to use effective contraception during treatment with Xenleta and for 2 days after the final dose (1).

The safety and effectiveness of Xenleta in pediatric patients less than 18 years of age have not been established (1).

Related policies
Baxdela, Nuzyra, Sivextro, Zyvox

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Xenleta may be considered **medically necessary** if the conditions indicated below are met.

Xenleta may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following

Community-Acquired Bacterial Pneumonia (CABP) caused by **OR** strongly suspected to be caused by **ONE** of the following:

1. *Chlamydophila pneumoniae*
2. *Haemophilus influenza*
3. *Legionella pneumophila*
4. *Mycoplasma pneumoniae*

5. *Staphylococcus aureus* (methicillin-susceptible)
6. *Streptococcus pneumoniae* (including MDRSP)

AND the following:

1. Inadequate treatment response, intolerance, or contraindication to a first-line antibiotic, such as a macrolide, fluoroquinolone, beta-lactam, or tetracycline

Prior – Approval *Renewal* Requirements

Same as above

Policy Guidelines

Pre - PA Allowance

Quantity 7 day supply every 365 days

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Xenleta (lefamulin) is a systemic pleuromutilin antibacterial. It inhibits bacterial protein synthesis through interactions with the A- and P-sites of the peptidyl transferase center (PTC) in domain V of the 23s rRNA of the 50S subunit. The binding pocket of the bacterial ribosome closes around the mutilin core for an induced fit that prevents correct positioning of tRNA. Xenleta is bactericidal against *S. pneumoniae*, *H. influenzae*, and *M. pneumoniae*, and bacteriostatic against *S. aureus* and *S. pyogenes* at clinically relevant concentrations (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Xenleta while maintaining optimal therapeutic outcomes.

References

1. Xenleta [package insert]. Dublin, Ireland: Nabriva Therapeutics US, Inc.; June 2021.

Policy History

Date	Action
January 2020	Addition to PA
March 2020	Annual review
December 2021	Annual review and reference update
December 2022	Annual review and reference update. Changed policy number to 5.01.055
June 2023	Annual review
June 2024	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 13, 2024 and is effective on July 1, 2024.