

**XENLETA
(lefamulin)****RATIONALE FOR INCLUSION IN PA PROGRAM****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).

**XENLETA
(lefamulin)****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.