Xenleta ™ (lefamulin) – New drug approval

- On August 19, 2019, the FDA announced the approval of Nabriva Therapeutics' Xenleta (lefamulin), 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*.

- CABP occurs when someone develops pneumonia in the community (not in a hospital). According to data from the Centers for Disease Control and Prevention, each year in the U.S., about one million people are hospitalized with CABP and 50,000 people die from the disease.

- Xenleta is a first-in-class semi-synthetic pleuromutilin antibiotic.

- The efficacy of Xenleta was established in two double-blind, double-dummy, non-inferiority studies in 1,289 adults with CABP. Study 1 compared 5 to 10 days of Xenleta to 7 to 10 days of moxifloxacin ± linezolid. Study 2 compared 5 days of Xenleta to 7 days of moxifloxacin. In both studies, efficacy was determined by Early Clinical Response (ECR) at 72 to 120 hours after the first dose. Response was defined as survival with improvement of at least two symptoms, no worsening of any symptom, and no receipt of non-study antibacterial treatment for CABP.

    — In study 1, ECR was achieved in 87.3% and 90.2% of patients in the Xenleta and moxifloxacin ± linezolid arms, respectively (difference: -2.9; 95% CI: -8.5, 2.8).
    — In study 2, ECR was achieved in 90.8% of patients in both the Xenleta and moxifloxacin arms (difference: 0.1; 95% CI: -4.4, 4.5).

- Xenleta is contraindicated in patients with known hypersensitivity to lefamulin, pleuromutilin class drugs, or any of the components of Xenleta; and concomitant use of Xenleta tablets with CYP3A substrates that prolong the QT interval is contraindicated.

- Warnings and precautions for Xenleta include QT prolongation, embryo-fetal toxicity, *Clostridium difficile*-associated diarrhea, and development of drug-resistant bacteria.

- The most common adverse reactions (≥ 2%) with Xenleta injection use were administration site reactions, hepatic enzyme elevation, nausea, hypokalemia, insomnia, and headache.

- The most common adverse reactions (≥ 2%) with Xenleta tablet use were diarrhea, nausea, vomiting, and hepatic enzyme elevation.

- The recommended dose of Xenleta is 150 mg every 12 hours by intravenous (IV) infusion over 60 minutes for 5 to 7 days or 600 mg orally every 12 hours for 5 days.

    — For patients starting with Xenleta IV, they may switch to Xenleta tablets 600 mg every 12 hours to complete the treatment course.

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- Nabriva plans to launch Xenleta in mid-September 2019. Xenleta will be available in a single-dose vial containing 150 mg of lefamulin and a 600 mg tablet.