Animal Health Advisory: Canine Cases of Extensively-Drug-Resistant *Pseudomonas aeruginosa*Linked to Multistate Outbreak Associated with Artificial Tears 10.17.2023

Dear Colleagues,

Two canine cases of a rare extensively-drug-resistant *Pseudomonas aeruginosa* were identified at a New Jersey veterinary facility. This bacterial strain has been linked to an ongoing multistate outbreak in humans, associated with artificial tear use. Prior to this multi-state outbreak, this bacterial strain has never been reported in the United States or in animals. To date, Los Angeles County has had zero reported cases in pets.

Key Points:

- EzriCare Artificial Tears, Delsam Pharma Artificial Tears, and Delsam Pharma Artificial Ointment have been associated with a multi-state outbreak of a rare strain of carbapenem resistant *Pseudomonas aeruginosa* (CRPA) in humans.
 - The full name of the bacterial strain is Verona Integron-mediated Metallo-β-lactamase (VIM) and Guiana-Extended Spectrum-β-Lactamase (GES)- producing carbapenem-resistant *Pseudomonas* aeruginosa (VIM-GES-CRPA).
- Two canine cases have been identified in New Jersey. One canine case was identified though a bronchoalveolar lavage and the other through an ear infection. Neither canine had known use of the products listed above or had close contact with a human case, therefore it is currently unknown how the canine cases were infected.
- Immediately discontinue use of EzriCare Artificial Tears, Delsam Pharma Artificial Tears, and Delsam Pharma Artificial Ointment, and monitor pets for signs of infection if these products were used on them.

Background:

As of May 15, 2023, CDC, in partnership with state and local health departments, identified 81 human patients in 18 states (CA, CO, CT, DE, FL, IL, NC, NJ, NM, NV, NY, OH, PA, SD, TX, UT, WA, WI) with VIM-GES-CRPA, a rare strain of extensively drug-resistant *P. aeruginosa*. Dates of specimen collection from human patients were from May 2022 to April 2023. Human case patients were identified from cultures of sputum, bronchial wash, or tracheal aspirate (14), sites related to the eye (cornea, vitreous; 21); urine (13); other nonsterile sources (3), blood (3), and ear (1); and from rectal swabs (26) collected for surveillance. Adverse outcomes associated with clinical (non-surveillance) cultures and reported to public health include 14 human patients with vision loss, an additional 4 patients with enucleation (surgical removal of eyeball), and 4 deaths within 30 days of VIM-GES-CRPA clinical culture collection.

Dates of specimen collection from the canine patients were in March and June 2023. Isolates were identified from bronchoalveolar lavage and ear cultures. Although most human cases have been associated with the implicated eye products or close contact with human case patients, neither dog nor respective household contacts had known exposure to artificial tears manufactured by Global Pharma or close contact with an identified case patient.

Isolates in this outbreak are sequence type (ST) 1203, harbor *bla*VIM-80 and *bla*GES-9 (a combination not previously observed in the United States) and are closely related based on analysis of whole genome sequencing (WGS) data.

These isolates are not susceptible to cefepime, ceftazidime, piperacillin-tazobactam, aztreonam, carbapenems, ceftazidime-avibactam, ceftolozane-tazobactam, fluoroquinolones, polymyxins, amikacin, gentamicin, and tobramycin; the subset of isolates that underwent antimicrobial susceptibility testing for cefiderocol were susceptible to this agent.

Action Items and Recommendations:

- Immediately discontinue use of EzriCare Artificial Tears, Delsam Pharma Artificial Tears, and Delsam Pharma Artificial Ointment in veterinary patients and advise owners who used EzriCare Artificial Tears on their pets to immediately discontinue and to monitor for signs of infection.
- Perform culture and antimicrobial susceptibility testing when clinically indicated. If cultures show antimicrobial resistance, request further characterization by a veterinary or animal health diagnostic laboratory.
 - Consider requesting carbapenem susceptibility testing if initial culture and susceptibility testing identifies extensively drug-resistant *P. aeruginosa*. When *P. aeruginosa* are identified that are resistant to carbapenems (imipenem, meropenem, or doripenem) and not susceptible to cefepime and ceftazidime, consider performing or submitting to a veterinary or animal health diagnostic laboratory that performs carbapenem resistance mechanism testing.
- Veterinarians treating patients for keratitis or endophthalmitis should ask owners if they
 have used EzriCare Artificial Tears on their pet(s). At this time it is not recommended to
 test animal patients who have used this product and who are not experiencing any signs
 or symptoms of infection. However, veterinarians should consider performing
 antimicrobial susceptibility testing and culture to help guide therapy in cases of
 persistent or unresolved infections, especially if owners report use of this product on
 their pets.
- Veterinarians treating VIM-GES-CRPA infections should **consult with a specialist** knowledgeable in the treatment of antibiotic-resistant bacteria to determine the best treatment option. Veterinary staff should use proper PPE when handling these patients

and also educate owners on proper PPE. At minimum, wear a mask, gloves and eye protection when handling these patients. It is best to also wear a gown that can be removed and discarded or laundered after use.

 Report any cases of VIM-GES-CRPA to Los Angeles County Veterinary Public Health using this form: http://publichealth.lacounty.gov/vet/docs/Forms/MDRO.pdf

Sincerely,

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