DELAWARE HEALTH ADVISORY #497: Outbreak of *Pseudomonas aeruginosa* Associated with Artificial Tears

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The Delaware Division of Public Health (DPH) is forwarding this advisory from the Centers for Disease Control and Prevention (CDC).

Summary

The Centers for Disease Control and Prevention (CDC) is issuing this Health Alert Network (HAN) Health Advisory about infections with an extensively drug-resistant strain of Verona Integron-mediated Metallo-β-lactamase (VIM) and Guiana-Extended Spectrum-β-Lactamase (GES)-producing carbapenem-resistant *Pseudomonas aeruginosa* (VIM-GES-CRPA) in 12 states. Most patients reported using artificial tears. Patients reported more than 10 different brands of artificial tears, and some patients used multiple brands. The majority of patients who used artificial tears reported using EzriCare Artificial Tears, a preservative-free, over-the-counter product packaged in multidose bottles. CDC laboratory testing identified the presence of the outbreak strain in opened EzriCare bottles with different lot numbers collected from two states. Patients and healthcare providers should immediately discontinue using EzriCare artificial tears pending additional guidance from CDC and the Food and Drug Administration (FDA).

Background

As of January 31, 2023, CDC in partnership with state and local health departments identified 55 case-patients in 12 states (CA, CO, CT, FL, NJ, NM, NY, NV, TX, UT, WA, WI) with VIM-GES-CRPA, a rare strain of extensively drug-resistant *P. aeruginosa*. Thirty-five patients are linked to four healthcare facility clusters. Dates of specimen collection were from May 2022 to January 2023. Isolates have been identified from clinical cultures of sputum or bronchial wash (13), cornea (11), urine (7), other nonsterile sources (4), blood (2), and from rectal swabs (25) collected for surveillance; some patients had specimens collected from more than one anatomic site. These specimens were collected in both outpatient and inpatient healthcare settings. Patients had a variety of presentations including keratitis, endophthalmitis, respiratory infection, urinary tract infection, and sepsis. Patient outcomes include permanent vision loss resulting from cornea infection, hospitalization, and one death due to systemic infection.

Review of common exposures revealed that most patients, including most patients with eye infections, used artificial tears prior to identification of VIM-GES-CRPA infection or colonization. Patients reported more than 10 brands of artificial tears, and some patients used multiple brands. The majority of patients who used artificial tears reported using EzriCare Artificial Tears, a preservative-free product dispensed in multidose bottles. This was the only common artificial tears product identified across the four healthcare facility clusters. CDC laboratory testing identified the presence of VIM-GES-CRPA in opened EzriCare Artificial Tears bottles from multiple lots; these bottles were collected from patients with and without eye infections in two states. These product-related VIM-GES-CRPA match the outbreak strain. VIM-GES-CRPA recovered from opened bottles could represent either bacterial contamination during use or during

the manufacturing process. Testing of unopened bottles of EzriCare Artificial Tears is ongoing to assist in evaluating for whether contamination may have occurred during manufacturing.

Recommendations for Health Care Providers

- Immediately discontinue using EzriCare Artificial Tears pending additional guidance from CDC and FDA.
- Advise patients who used EzriCare Artificial Tears to monitor for signs and symptoms of infection. Perform culture and antimicrobial susceptibility testing when clinically indicated.
- Healthcare providers treating patients for keratitis or endophthalmitis should ask patients if they have used EzriCare Artificial Tears. Providers should consider performing culture and antimicrobial susceptibility testing to help guide therapy if patients report use of this product.
- Healthcare providers treating VIM-GES-CRPA infections should consult with a specialist knowledgeable in the treatment of antibiotic-resistant bacteria to determine the best treatment option. VIM-GES-CRPA isolates associated with this outbreak are extensively drug-resistant. Isolates that underwent susceptibility testing at public health laboratories were not susceptible to cefepime, ceftazidime, piperacillin-tazobactam, aztreonam, carbapenems, ceftazidime-avibactam, ceftolozane-tazobactam, fluoroquinolones, polymyxins, amikacin, gentamicin, and tobramycin. A subset of 3 isolates that underwent antimicrobial susceptibility testing for cefiderocol at clinical laboratories or CDC were susceptible to this agent.
- Place patients infected or colonized with VIM-GES-CRPA and admitted to acute care settings in isolation and use Contact Precautions. For residents of skilled nursing facilities who are infected or colonized with VIM-GES-CRPA, use Enhanced Barrier Precautions if the resident does not have an indication for Contact Precautions.
- At this time, CDC does not recommend testing patients who have used this product and who are not experiencing any signs or symptoms of infection.

Reporting

Infections can be reported to the DPH Office of Infectious Disease Epidemiology (OIDE). Cases can be reported by phone (302-744-4990, normal business hours; 1-888- 295-5156, outside of normal business hours), fax (302-622-4149), or email (reportdisease@delaware.gov).

Recommendations for Clinical Laboratories

Isolates in this outbreak are sequence type (ST) 1203, harbor *bla*$_{\text{VIM-80}}$ and *bla*$_{\text{GES-9}}$ (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.

- Clinical laboratories that identify *P. aeruginosa* resistant to imipenem or meropenem are encouraged to perform carbapenem resistance mechanism testing; isolates may also be submitted to the Antimicrobial Resistance Laboratory Network for mechanism testing.
    - Laboratories wishing to apply a more specific definition when identifying isolates that might be related to this cluster for mechanism testing could limit testing to carbapenem-resistant *P. aeruginosa* that are also resistant to cefepime, ceftazidime, and (if tested) ceftazidime-avibactam and ceftolozane-tazobactam.
- Clinical laboratories that identify any carbapenem-resistant *P. aeruginosa* from an ocular specimen or VIM-CRPA from any specimen source should submit the isolate to the Delaware Public Health Laboratory for further characterization. For assistance submitting isolates, call 302-744-4900 (normal business hours), 1-888-295-5156 (outside of normal business hours), fax 302-622-4149, or email reportdisease@delaware.gov.

For More Information

- CRPA Outbreak Linked to Artificial Tears
- Antimicrobial Resistance Laboratory Network
- Visit CDC-INFO or call CDC-INFO at 1-800-232-4636
- CDC 24/7 Emergency Operations Center (EOC) 770-488-7100