MLS Laboratory Update: Update on Carbapenem-resistant *Pseudomonas aeruginosa* National Investigation

FEBRUARY 10, 2023

Purpose of this Message:

To provide MLS laboratorians with an update on the national investigation into carbapenemase-producing, carbapenem-resistant *Pseudomonas aeruginosa* (CP-CRPA) associated with the use of EzriCare Artificial Tears and to request that laboratories submit isolates of CRPA and CP-CRPA to MDH-PHL.

Action Item:

Request for Clinical Laboratories

- Please submit *P. aeruginosa* isolates:
  - from any source
  - that are resistant to imipenem or meropenem, cefepime, ceftazidime,
    - and if tested, ceftazidime-avibactam and ceftolozane-tazobactam
  - if your laboratory performs carbapenemase testing and the isolate is a carbapenemase-producer, or more specifically VIM-producing
- If your laboratory does not perform carbapenemase testing and has the above resistance pattern, MDH-PHL will perform and report carbapenemase testing on submitted isolates
- When submitting isolates use the following forms:
  - AR Lab Central Region Lab Testing and Submission Form (www.health.state.mn.us/diseases/idlab/arln.html)
  - CRO Isolate – Supplemental Submission Form (if necessary) (https://www.health.state.mn.us/diseases/idlab/arln.html)

Background:

Brief: The Centers for Disease Control and Prevention (CDC) is investigating a national cluster of 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). At this time no VIM-GES-CRPA isolates matching the multi-state cluster have been detected in Minnesota.

Additional Background: As of January 31, 2023, CDC, in partnership with state and local health departments, has 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.

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.

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 whether contamination may have occurred during manufacturing.

Recommendations for Healthcare 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. Send isolates to the Minnesota Department of Health Public Health (MDH-PHL) laboratory.
- 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 (https://www.cdc.gov/infectioncontrol/guidelines/isolation/index.html). For residents of skilled nursing facilities who are infected or colonized with VIM-GES-CRPA, use Enhanced Barrier Precautions (https://www.cdc.gov/hai/containment/PPE-Nursing-Homes.html) 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.

Recommendations for the Public

- Discontinue using EzriCare Artificial Tears pending additional guidance from CDC and FDA.
- If patients were advised to use EzriCare Artificial Tears by their healthcare provider, they should follow up with their healthcare provider for an alternative artificial tears product to use.
- Patients who used EzriCare Artificial Tears and who have signs or symptoms of an eye infection, such as discharge from the eye, eye pain or discomfort, redness of the eye or eyelid, feeling of something in the eye, increased sensitivity to light, or blurry vision, should seek timely medical care. CDC does not currently recommend testing of patients who have used this product and who are not experiencing any signs or symptoms of infection.

Additional Information:

- Outbreak of Extensively Drug-resistant Pseudomonas aeruginosa Associated with Artificial Tears (https://www.cdc.gov/hai/outbreaks/crpa-artificial-tears.html)
- Health Alert Network (HAN) - 00485 | Outbreak of Extensively Drug-resistant Pseudomonas aeruginosa Associated with Artificial Tears (https://emergency.cdc.gov/han/2023/han00485.asp)
- FDA warns consumers not to purchase or use EzriCare Artificial Tears due to potential contamination | FDA (https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-consumers-not-purchase-or-use-ezricare-artificial-tears-due-potential-contamination)
- MedWatch: The FDA Safety Information and Adverse Event Reporting Program | FDA (https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program)

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Thank you for your assistance with this investigation,

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