DATE
February 3, 2023

SUBJECT
Outbreak of Extensively Drug-resistant Pseudomonas aeruginosa
Associated with Artificial Tears

INSTRUCTIONS
DISTRIBUTE to your local HAN contacts. This HAN is intended for general sharing of information.
- Time for Forwarding: As Soon As Possible
- Please forward to DPHHS at hhshan@mt.gov
- Remove this cover sheet before redistributing and replace it with your own

For LOCAL HEALTH DEPARTMENT reference only
DPHHS Subject Matter Resource for more information regarding this HAN, contact:
DPHHS CDCP Epidemiology Section
1-406-444-0273

Immunization Section
1-406-444-5580

For technical issues related to the HAN message contact the Emergency Preparedness Section at 1-406-444-0919

DPHHS HAN Website:
https://dphhs.mt.gov/publichealth/phep/han

Please ensure that DPHHS is included on your HAN distribution list.
hhshan@mt.gov

Categories of Health Alert Messages:
- Health Alert: provides vital, time-sensitive information for a specific incident or situation; warrants immediate action or attention by health officials, laboratorians, clinicians, and members of the public; and conveys the highest level of importance.
- Health Advisory: provides important information for a specific incident or situation; contains recommendations or actionable items to be performed by public health officials, laboratorians, and/or clinicians; may not require immediate action.
- Health Update: provides updated information regarding an incident or situation; unlikely to require immediate action.
- Information Service: provides general public health information; unlikely to require immediate action.

Please update your HAN contact information in the Montana Public Health Directory.
DATE
February 3, 2023

SUBJECT
Multistate VIM-GES carbapenem-resistant *Pseudomonas aeruginosa* outbreak

BACKGROUND
The Montana Department of Public Health and Human Services (DPHHS) has not identified an isolate of VIM-GES carbapenem-resistant *Pseudomonas aeruginosa* in Montana as of 2/2/2023.

INFORMATION
See CDC HAN 00485

RECOMMENDATIONS
Please refer to the recommendations in the CDC HAN message. In addition, please see Montana-specific laboratory and healthcare provider recommendations below.

**Recommendations for Clinical Laboratories in Montana:**

- As a reminder, Carbapenem-Resistant Organisms (CROs) are included on the “Confirmation of Disease” list under Administrative Rule of Montana 37.114.313 ([37.114.313 : CONFIRMATION OF DISEASE - Administrative Rules of the State of Montana (mt.gov)]). Specimens that meet this criteria should be sent to the Montana Public Health Laboratory for additional testing.
- Please send carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) isolates, and other resistant isolates of interest, to the Montana Public Health Laboratory (MTPHL) so further surveillance testing can be performed. Please do not send specimens directly to CDC Antimicrobial Resistance Laboratory Network (ARLN) laboratories, as directed in the CDC HAN below. This allows DPHHS to track drug resistant organisms in Montana and alert public health to any cases that may be linked to known clusters around the state and/or nation. If further testing is needed, MTPHL will send specimens to CDC ARLN laboratories.
- As a reminder, please include antimicrobial sensitivities from your facility along with the submitted isolate. You can order Carbapenem-resistant *Pseduomonas* (CRPA) Testing using the online lab portal ([Montana Public Health Lab (mt.gov)]). Be sure to add any additional information, such as exposure or link to outbreak if known, in the available comment section.
- For questions call the Montana Public Health Laboratory 1-800-821-7284.
Recommendations for Healthcare Providers:

- Please see the healthcare provider recommendations below in the CDC HAN.
- Report suspect cases to your local public health jurisdiction (https://dphhs.mt.gov/publichealth/FCSS/countytribalhealthdepts).
- Notify your local health jurisdiction prior to sending specimens to the Montana Public Health Laboratory so specimens can be prioritized for outbreak testing.

Healthcare facilities, providers, and local public health jurisdictions can contact Erika Baldry, Infection Control and Prevention/Healthcare-Associated Infections Section, at 406-444-0275.
CDC HEALTH ADVISORY

Outbreak of Extensively Drug-resistant *Pseudomonas aeruginosa* Associated with Artificial Tears

**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.

Isolates in this outbreak are sequence type (ST) 1203, harbor bla\textsubscript{VIM-80} and bla\textsubscript{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 for 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.
- 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 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.

Recommendations for Clinical Laboratories

- 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 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 Antimicrobial Resistance Laboratory Network for further characterization. Please reach out to your health department's healthcare-associated infections contact or email haioutbreak@cdc.gov for assistance submitting isolates.

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. At this time, CDC does not recommend testing of patients who have used this product and who are not experiencing any signs or symptoms of infection.

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
The Centers for Disease Control and Prevention (CDC) protects people’s health and safety by preventing and controlling diseases and injuries; enhances health decisions by providing credible information on critical health issues; and promotes healthy living through strong partnerships with local, national, and international organizations.

<table>
<thead>
<tr>
<th>Categories of Health Alert Network messages</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Health Alert</td>
<td>Requires immediate action or attention. Conveys the highest level of importance about a public health event.</td>
</tr>
<tr>
<td>Health Advisory</td>
<td>Requires immediate action. Provides important information about a public health event.</td>
</tr>
<tr>
<td>Health Update</td>
<td>May require immediate action. Provides updated information about a public health event.</td>
</tr>
<tr>
<td>HAN Info Service</td>
<td>Does not require immediate action. Provides general information about a public health event.</td>
</tr>
</tbody>
</table>

This message was distributed to state and local health officers, state and local epidemiologists, state and local laboratory directors, public information officers, HAN coordinators, and clinician organizations.