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Physician Alert

Clinical Practice Change: Clinical Microbiology

Date: February 12, 2013

To: Infectious Diseases Physicians and Infection Prevention and Control

From: Dr. Michelle Alfa, Medical Director, Clinical Microbiology Discipline, DSM

Re: **Changes to Third-Generation Cephalosporin AST Result Reporting for Enterobacteriaceae**

TAKE HOME MESSAGE:
Effective January 10, 2013 isolates of *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, and *Proteus mirabilis* containing an extended spectrum beta lactamase (ESBL) may be reported as susceptible to ceftriaxone or ceftazidime based upon new Clinical and Laboratory Standards Institute (CLSI) testing and reporting guidelines.

In January 2010, the Clinical and Laboratory Standards Institute (CLSI) lowered MIC (susceptibility) breakpoints for cefazolin, cefotaxime, ceftizoxime, ceftriaxone, ceftazidime, and aztreonam for Enterobacteriaceae in order to better reflect the activities of these agents when used to treat patients with infections caused by contemporary isolates with currently recommended dosage regimens. Clinical laboratories dependent upon automated systems (e.g., Vitek, MicroScan) to perform antimicrobial susceptibility testing (AST) were unable to implement these changes immediately because of the absence of FDA clearance and lack of appropriate dilutions in the panels used for AST. Following this delay the new lower breakpoints were validated and implemented for reporting patient results in DSM laboratories on January 10, 2013.

Previous CLSI recommendations to perform ESBL screening and confirmatory tests to change penicillin, cephalosporin, and aztreonam results from susceptible to resistant for isolates with a positive ESBL confirmatory test were based upon observations that some ESBL-producing isolates demonstrated elevated but susceptible MICs (using former breakpoints) to these agents and resulted in poorer outcomes in patients with infections due to isolates harbouring ESBLs (Paterson DL et al., J Clin Microbiol 2001;39:2206–12). ESBL screening and confirmatory testing recommendations were always intended to be a short-term solution to address a new mechanism of resistance.

DSM laboratories continue to perform ESBL screening and confirmatory tests for Infection Prevention and Control (IP&C) purposes only. Given this continued testing, there is potential for an isolate of *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, or *Proteus mirabilis* (species of Enterobacteriaceae screened for ESBLs) to be ESBL-positive and susceptible to either ceftriaxone or ceftazidime depending upon the spectrum of activity of the specific ESBL.

DSM has revised its reporting comment for ESBL-producing Enterobacteriaceae to "This isolate contains an extended spectrum beta lactamase (ESBL). This isolate should be considered clinically resistant to penicillins and aztreonam; susceptibility to specific cephalosporins should be based upon their in vitro susceptibility testing results. Consultation with the Infectious Disease Service is recommended. Follow the Infection Prevention and Control guidelines for Antibiotic Resistant Organisms (ARO)."

Based upon MIC distribution data, it is anticipated that the lowered breakpoints for ceftriaxone and ceftazidime will only have a modest effect on the susceptibility rates for Enterobacteriaceae that will be reported in the 2014 antibiogram (based upon 2013 data). It is expected that the lowered breakpoints for cefazolin will have a more substantive impact on susceptibility for Enterobacteriaceae in the 2014 antibiogram.

If you have any questions, please contact Dr. M. Alfa at (204) 237-2105.