



## Beta-lactamases: Focus on Carbapenemases

In previous KASIC pearls, we reviewed the [basics of  \$\beta\$ -lactamases](#) as well as the commonly encountered [ESBLs](#) and [AmpC  \$\beta\$ -lactamases](#). But what about the enzymes that destroy our broad spectrum carbapenems? Let's take a closer look at the increasingly concerning group of enzymes called the carbapenemases.

### What is a Carbapenemase?

Carbapenemases are enzymes that inactivate nearly all  $\beta$ -lactams including carbapenems.<sup>1</sup> There are various different types of carbapenemases that come from different genes. The most common carbapenemase in the United States is the *Klebsiella pneumoniae* carbapenemase (KPC). Of note, KPC can be produced by many bacteria, not just *K. pneumoniae*.

### How are Carbapenemases Identified?

Carbapenemases can be identified phenotypically (e.g. CarbaNP test) and genotypically (e.g. PCR); but these tests are not always available in clinical microbiology laboratories. Some bacteria are resistant to carbapenems through other mechanisms.

### Treatment of Carbapenemase Infections

The treatment of carbapenem resistant organisms is generally guided by susceptibility testing. Identifying which carbapenemase gene is present may help guide therapy. The Infectious Diseases Society of America provides recommendations for the management of infections due to carbapenem-resistant Enterobacterales (e.g. *E. coli*, *K. pneumoniae*) according to the source of the infection as summarized in the table below.<sup>3</sup>

Uncomplicated Cystitis	Pyelonephritis and Complicated UTI	Outside the Urinary Tract		
		KPC or no carbapenemase testing	OXA-48	Metallo- $\beta$ -lactamase (NDM, VIM, IMP)
<b>Preferred:</b> Nitrofurantoin Ciprofloxacin Levofloxacin TMP-SMX  <b>Alternatives:</b> <a href="#">Aminoglycoside x1</a> Fosfomycin N-BL/BLI* Colistin Cefiderocol	<b>Preferred:</b> Ciprofloxacin Levofloxacin TMP-SMX N-BL/BLI* Cefiderocol  <b>Alternatives:</b> Aminoglycosides	<b>Preferred:</b> Ceftazidime-avibactam* Meropenem-vaborbactam* Imipenem-cilastatin-relebactam*  <b>Alternatives:</b> Cefiderocol	<b>Preferred:</b> Ceftazidime-avibactam  <b>Alternatives:</b> Cefiderocol	<b>Preferred:</b> Cefiderocol Ceftazidime-avibactam plus <a href="#">aztreonam</a>
<b>Alternatives:</b> Tigecycline†, Eravacycline†				

\*Novel  $\beta$ -lactam/ $\beta$ -lactamase (N-BL/BLI) combination

†Not suggested for urinary tract infections or bloodstream infections

**Key Takeaway:** The treatment of carbapenemase producing organisms should be guided by site of infection, susceptibility testing, and genetic markers (if known). Non- $\beta$ -lactam alternatives should be used whenever possible to preserve novel  $\beta$ -lactam/ $\beta$ -lactamases and avoid inducing further  $\beta$ -lactam resistance.

### References:

1. Queenan AM, Bush K. Carbapenemases: the versatile beta-lactamases. Clin Microbiol Rev. 2007;20(3):440-458.
2. Vázquez-Ucha JC, Arca-Suárez J, Bou G, Beceiro A. New Carbapenemase Inhibitors: Clearing the Way for the  $\beta$ -Lactams. Int J Mol Sci. 2020;21(23):9308.
3. Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Antimicrobial-Resistant Treatment Guidance: Gram-Negative Bacterial Infections. Infectious Diseases Society of America 2023; Version 3.0. Available at <https://www.idsociety.org/practice-guideline/amr-guidance/>. Accessed 29 December 2023.