Antimicrobials with and without activity against carbapenemase-producing Enterobacterales

This table provides a summary of the enzymes most commonly responsible for carbapenem resistance in Enterobacterales and lists antimicrobials that are likely to have activity, that may have activity, and that do not or are unlikely to have activity against these enzymes. The antimicrobials that are unlikely to have activity against CPEs should not be used.

Drug choice (including whether combination therapy is required) will depend on the site of infection, infection severity and the causative organism – seek advice from a clinical microbiologist or infectious diseases physician. It may be necessary to modify therapy once the results of susceptibility testing are available – expert advice may be needed.

Resistance mechanism	Antimocrobials that are likely to have activity [NB1]	Antimicrobials that may have activity [NB2]	Antimicrobials without or unlikely to have activity [NB3]
KPC, GES	amikacin aztreonam+avibactam [NB4] ceftazidime+avibactam cefiderocol eravacycline meropenem+vaborbactam	colistin [NB5] polymyxin B [NB6] tobramycin gentamicin fosfomycin tigecycline imipenem+cilastatin+relebactam trimethoprim+sulfamethoxazole	aztreonam carbapenems [NB7] cephalosporins other than cefiderocol and ceftazidime+avibactam ciprofloxacin penicillins penicillins+beta-lactamase inhibitors (eg amoxicillin+clavulanate)
OXA-48 type	amikacin ceftazidime+avibactam cefiderocol eravacycline gentamicin tobramycin	ciprofloxacin aztreonam ceftolozane+tazobactam colistin [NB5] polymyxin B [NB6] fosfomycin tigecycline meropenem [NB7] trimethoprim+sulfamethoxazole	cephalosporins other than cefiderocol, ceftolozane+tazobactam and ceftazidime+avibactam penicillins penicillins+beta-lactamase inhibitors (eg amoxicillin+clavulanate)
IMP, NDM, VIM	amikacin aztreonam+avibactam [NB4] cefiderocol eravacycline	aztreonam ciprofloxacin gentamicin tobramycin colistin [NB5] polymyxin B [NB6] fosfomycin tigecycline trimethoprim+sulfamethoxazole	cephalosporins other than cefiderocol penicillins penicillins+beta-lactamase inhibitors (eg amoxicillin+clavulanate) meropenem [NB7]

Key:

CPE = carbapenemase-producing Enterobacterales; GES = Guiana extended-spectrum beta-lactamase; IMP = imipenemase; KPC = Klebsiella pneumoniae carbapenemase; NDM = New Delhi metallo-beta-lactamase; OXA-48 = oxacillinase-48; VIM = Verona-Integron encoded metallo-beta-lactamase

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NB1: This list is not exhaustive. Rather, it includes antimicrobials available in Australia at the time of writing (including via the Special Access Scheme) that have been suggested in the literature and by Australian epidemiological data to retain activity against CPEs. A patient's isolate may not be susceptible to all listed antibiotics because of co-resistance.

NB2: This list is not exhaustive. Rather, it includes antimicrobials available in Australia at the time of writing (including via the Special Access Scheme) that have been shown to have activity against CPEs. However, antimicrobials that may have activity against CPEs includes some that cannot be used in the treatment of specific Enterobacterales species because of intrinsic resistance. For example, colistin, imipenem+relebactam and tigecycline cannot be used to treat infection caused by Morganella, Proteus and Providencia species.

NB3: This list is not exhaustive. Rather, it includes antimicrobials available in Australia at the time of writing (including via the Special Access Scheme) that do not have or unlikely to have activity CPEs.

NB4: Aztreonam+avibactam is not registered for use in Australia but is available via the Special Access Scheme. In practice, ceftazidime+avibactam PLUS aztreonam is used as an alternative. At the time of writing, no standardised laboratory testing to determine susceptibility to aztreonam+avibactam is available.

NB5: Dosing colistin according to the product information does not result in therapeutic concentrations. Updated dosing advice can be found in the *International Consensus Guidelines for the Optimal Use of the Polymyxins* (https://pubmed.ncbi.nlm.nih.gov/30710469/)

NB6: Polymyxin B should not be used to treat urinary tract infections as it is not excreted by the kidneys.

NB7: Carbapenems are occasionally used without beta-lactamase inhibitors to treat infections caused by CPEs. This should only be considered when the minimum inhibitory concentration (MIC) of the carbapenem is low and other options for treatment are not available. When used without beta-lactamase inhibitors, carbapenems are usually combined with another antimicrobial with activity against CPEs; consideration should also be given to optimising antimicrobial exposure (eg use of extended infusions).