

treatment, for acute pyelonephritis, has been shown to be equivalent to longer durations of therapy in terms of clinical and microbiological success. However, this is associated with a higher recurrence rate of infection within four to six weeks and needs to be tailored to local policies and resistance patterns [234].

3.6.3.2 Inpatient treatment

Patients with pyelonephritis requiring hospitalisation should be treated initially with an intravenous antimicrobial regimen e.g. a fluoroquinolone, an aminoglycoside (with or without ampicillin), or an extended-spectrum cephalosporin or penicillin [235]. Ceftolozane/tazobactam achieved a clinical response rate of over 90% in patients with pyelonephritis [236, 237]. It also demonstrated significantly higher composite cure rates than levofloxacin among levofloxacin-resistant pathogens [238]. Ceftazidime-avibactam combination has been shown to be effective for treating ceftazidime-resistant *Enterobacterales* and *Pseudomonas aeruginosa* UTIs [239].

Novel antimicrobial agents include imipenem/cilastatin, cefiderocol, meropenem-vaborbactam and plazomicin. Imipenem/cilastatin has been investigated in a phase 2 randomised trial and showed good clinical response rates [240]. Cefatazidime-avibactam and doripenem showed similar efficacy against ceftazidime non-susceptible pathogens and may offer an alternative to carbapenems in this setting [241]. Meropenem-vaborbactam has been shown to be non-inferior to piperacillin-tazobactam in a phase 3 RCT [242]. It was also effective for treating carbapenem-resistant *Enterobacterales* with cure rates of 65% compared to best available treatment [243]. Once daily plazomicin was non-inferior to meropenem for the treatment of complicated UTIs and acute pyelonephritis caused by *Enterobacterales*, including multidrug-resistant strains [244]. Cefiderocol was non-inferior to imipenem/cilastatin for the treatment of complicated UTI in people with multidrug-resistant Gram-negative infections in a phase 2 RCT [245].

Carbapenems and novel broad spectrum antimicrobial agents should only be considered in patients with early culture results indicating the presence of multi-drug resistant organisms. The choice between these agents should be based on local resistance patterns and optimised on the basis of drug susceptibility results. In patients presenting with signs of urosepsis, empiric antimicrobial coverage for ESBL-producing organisms is warranted [246]. Patients initially treated with parenteral therapy who improve clinically and can tolerate oral fluids may transition to oral antimicrobial therapy [247].

3.6.3.3 Summary of evidence and recommendations for the treatment of pyelonephritis

Summary of evidence	LE
Fluoroquinolones and cephalosporines are the only microbial agents that can be recommended for oral empirical treatment of pyelonephritis.	1b
Intravenous antimicrobial regimens for pyelonephritis may include a fluoroquinolone, an aminoglycoside (with or without ampicillin), or an extended-spectrum cephalosporin or penicillin.	1b
Carbapenems should only be considered in patients with early culture results indicating the presence of multi-drug resistant organisms.	4
The appropriate antimicrobial should be chosen based on local resistance patterns and optimised on the basis of drug susceptibility results.	3

Recommendations	Strength rating
Treat patients with pyelonephritis not requiring hospitalisation with short course fluoroquinolones as first-line treatment.	Strong
Treat patients with pyelonephritis requiring hospitalisation with an intravenous antimicrobial regimen initially.	Strong
Switch patients initially treated with parenteral therapy, who improve clinically and can tolerate oral fluids, to oral antimicrobial therapy.	Strong
Do not use nitrofurantoin, oral fosfomycin, and pivmecillinam to treat pyelonephritis.	Strong