



Fosfomycin: An Option for Pyelonephritis?

Oral fosfomycin 3 g once is a first-line recommended therapy for cystitis in the 2011 Infectious Diseases Society of America (IDSA) urinary tract infections (UTI) guidelines. The guidelines note that fosfomycin should be avoided where there is concern for early pyelonephritis.¹ However, there are reports of clinical success with oral fosfomycin in treating pyelonephritis and other UTIs with systemic signs of infection.²⁻⁴ Fosfomycin is often active against *E. coli* resistant to other antibiotics (e.g. [ESBLs](#)) and has the added advantage of oral administration.⁵ Could fosfomycin have a larger role to play in UTI therapy?

What does other guidance say?

The 2024 IDSA gram-negative resistance guidance document suggests against fosfomycin for pyelonephritis or other complicated urinary tract infections due to ESBL *E. coli*, however they note it may be a **reasonable option** when other preferred or alternative oral options are not available.⁶ Fosfomycin may avoid unnecessary line placement, especially after discharge.

What is the evidence?

Fosfomycin was non-inferior to ciprofloxacin in a randomized controlled trial as oral stepdown therapy following IV antibiotics for febrile urinary tract infections due to *E. coli*. Patients received IV lead in therapy for a mean of approximately 3 days followed by either fosfomycin dosed as 3 g q24h or ciprofloxacin 500 mg q12h for 10 days of total therapy. Rate of clinical cure at day 6-10 post therapy was 75% (36/48) in the fosfomycin arm and 65.2% (30/46) in the ciprofloxacin arm. There was no difference detected in clinical cure, reinfection, or relapse at 30-35 days post end of therapy. Notably, approximately 50% of patients in both groups were bacteremic at baseline. However, gastrointestinal adverse events were more common with the use of fosfomycin.³

In another small trial, fosfomycin 3 g q24h was compared to levofloxacin 750 mg daily for 5-7 days with up to 2 days of IV antibiotic lead in therapy in complicated urinary tract infections, most of which were pyelonephritis. Bacteremic patients were excluded. Similar rates of clinical cure were observed at end of therapy and test of cure approximately 21 days after antibiotic start.⁴

Does fosfomycin ONLY work against *E. coli*?

Fosfomycin [breakpoints](#) from CLSI exist for *E. coli* and *Enterococcus faecalis* for UTIs only. There is concern for increased risk for treatment failure with non-*E. coli* gram negatives due to the presence of certain resistance genes not common in *E. coli*.⁷ Routine susceptibility testing is not commonly done for fosfomycin.⁵ Contact your local microbiology laboratory to discuss procedures on testing for and [reporting](#) fosfomycin susceptibility.

Key Takeaway: Oral stepdown with fosfomycin has been used to treat UTIs with systemic signs of infection such as pyelonephritis due to *E. coli*, but may require repeat dosing. Fosfomycin may avoid line placement if other oral antibiotics are not an option.

References

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