



Burning Evidence for Fosfomycin in Cystitis

Clinical Question: What is the efficacy of fosfomycin for uncomplicated cystitis in non-pregnant women?

Bottom Line: At best, single dose fosfomycin has similar efficacy to other antibiotics for uncomplicated cystitis. However, the best quality, publicly funded trial showed it was not as efficacious as nitrofurantoin, with 58% of cases clinically resolving at 28 days compared to 70% for nitrofurantoin.

Evidence:

- Most recent systematic review¹, 11 randomized controlled trials (RCTs), 1976 women, fosfomycin versus other antibiotics (examples norfloxacin, trimethoprim/sulfamethoxazole, nitrofurantoin) showed:
 - Clinical cure or improvement (non-complete symptom resolution): no difference.
 - Limitations: unreliable results (combined cure and failure rates together in the same analysis), most studies over 20 years old and industry sponsored.
 - Focusing on 4 heaviest weighted RCTs (make up >85% of outcomes in systematic review):
 - Most recent, highest quality, publicly funded, open-label RCT² of fosfomycin versus nitrofurantoin in 494 women. At 28 days:
 - Clinical resolution: 58% versus 70% nitrofurantoin, number needed to harm=8.
 - Adverse events: no difference.
 - Manufacturer-sponsored, double-blind RCT³ of fosfomycin versus nitrofurantoin in 231 women:
 - Cured or improved: no difference at Day 4, 9, or 42.
 - Stopped due to adverse events: 6% versus 0 nitrofurantoin (mainly gastrointestinal).
 - Limitations: unable to track all patient outcomes, study is 27 years old, not all randomized patients included in analysis.
 - “Worst-case” analysis accounting for missing data resulted in statistically fewer patients improving by Day 9: 84% versus 95% nitrofurantoin.
 - Manufacturer-sponsored double-blind RCT⁴ of fosfomycin versus nitrofurantoin in 521 women:
 - Cured: no difference up to 6 weeks after treatment.

- Stopped due to adverse events: 2.6% versus 6.3% nitrofurantoin (not statistically different).
- Limitations: not all randomized patients included in analysis, single author, study is 21 years old.
- Second heaviest weighted RCT⁵: primary outcome was rectal cultures, not relevant.

Context:

- Guidelines recommend nitrofurantoin, fosfomycin, or trimethoprim/sulfamethoxazole (if low risk of resistance) as empiric first-line treatment for uncomplicated cystitis in women.^{6,7}
- Fosfomycin is a single-dose, orange-flavoured, powder sachet for dissolution in cold water.⁸
- Pricing: fosfomycin ~\$30, nitrofurantoin ~\$20 (5 days).⁹
- No renal adjustments required for fosfomycin.⁸

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Disclosures:

Authors do not have any conflicts of interest to declare.

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