



## Single-Dose Aminoglycoside for Cystitis: An Oldie but Goodie

Urinary tract infections (UTI) are one of the most common indications for antibiotics.<sup>1</sup> However, increasing antimicrobial resistance rates are limiting options for treatment. Aminoglycosides were introduced to the market in the 1940s and continue to have high rates of activity against uropathogens including those that are resistant to beta-lactams, fluoroquinolones, and trimethoprim-sulfamethoxazole.<sup>1</sup> Aminoglycoside use, however, has decreased during the last few decades due to concerns for adverse events such as nephrotoxicity and ototoxicity.<sup>2</sup>

With increasing rates of antimicrobial resistance, the utility of single-dose aminoglycosides has re-emerged.<sup>1</sup>

### Why are single dose aminoglycosides an ideal option for cystitis?

- Primarily excreted in the urine (85%-95%) with therapeutic levels for several days<sup>1</sup>
- Intramuscular (IM) or intravenous (IV) administration allows for emergency department and clinic availability
- Reduces hospital admission rates for longer courses of IV antibiotics when no oral options exist<sup>1</sup>
- No concern for lack of adherence to oral antibiotics
- Low risk for *Clostridioides difficile* infection due to lack of penetration into the gut lumen<sup>3</sup>
- Serum drug level monitoring not needed
- Toxicity risk minimal with single dose<sup>1</sup>

### What's the data?

Goodlet and colleagues reviewed 13 studies including 13,804 patients receiving single-dose aminoglycosides for UTI. The overall microbiologic cure rate was 94.5% ± 4.3%. Among those studies that had comparator arms, microbiologic cure rates for aminoglycosides and comparators were 95.4% ± 4.2% and 95.6% ± 3.9% respectively (p=0.76). The clinical cure, reported in only two studies, was 82.8% and 94.7%. The sustained microbiologic cure rate at 30 days was 73.4% ± 9.6%. The aminoglycoside adverse event rate across all studies was 0.5% (64/13,804). In comparative studies, the reported adverse event rate among alternatives was 3.5% (8/226).<sup>1</sup>

### Do the guidelines recommend it?

The 2022 IDSA gram negative resistance guidelines recommended single dose aminoglycoside as an alternative option for treatment of uncomplicated cystitis caused by resistant gram negative bacteria (e.g. ESBL, AmpC, CRE).<sup>4,5</sup>

**Cystitis dosing:** 5 mg/kg/dose for gentamicin or tobramycin and 15 mg/kg/dose for amikacin.<sup>4,5</sup> Use adjusted body weight instead of total body weight (TBW) if TBW > 120% ideal body weight.

**Key takeaway:** Single-dose aminoglycosides are an option in uncomplicated cystitis and have several advantages over alternatives

### References:

1. Goodlet KJ, Benhalima FZ, Nailor MD. A Systematic Review of Single-Dose Aminoglycoside Therapy for Urinary Tract Infection: Is It Time To Resurrect an Old Strategy? *Antimicrob Agents Chemother*. 2018 Dec 21;63(1):e02165-18. doi: 10.1128/AAC.02165-18. PMID: 30397061; PMCID: PMC6325212.
2. Vidal L, Gafter-Gvili A, Borok S, Fraser A, Leibovici L, Paul M. Efficacy and safety of aminoglycoside monotherapy: systematic review and meta-analysis of randomized controlled trials. *J Antimicrob Chemother*. 2007 Aug;60(2):247-57. doi: 10.1093/jac/dkm193. Epub 2007 Jun 11. PMID: 17562680.
3. Staley C, Vaughn BP, Graiziger CT, Sadowsky MJ, Khoruts A. Gut-sparing treatment of urinary tract infection in patients at high risk of *Clostridium difficile* infection. *J Antimicrob Chemother*. 2017;72(2):522-528. doi:10.1093/jac/dkw499
4. Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of Extended-Spectrum  $\beta$ -lactamase Producing Enterobacterales (ESBL-E), Carbapenem-Resistant Enterobacterales (CRE), and *Pseudomonas aeruginosa* with Difficult-to-Treat Resistance (DTR-P. *aeruginosa*). *Clin Infect Dis*. 2021 Apr 8;72(7):e169-e183. doi: 10.1093/cid/ciaa1478. PMID: 33106864.
5. Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -Lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. *Clin Infect Dis*. 2022 Jul 6;74(12):2089-2114. doi: 10.1093/cid/ciab1013. PMID: 34864936.