



Know your Antibiotic: Nitrofurantoin

Nitrofurantoin is a nitrofuran antibiotic that requires activation by bacterial enzymes resulting in inhibition of protein synthesis, bacterial DNA damage, metabolic disruption, and cell wall synthesis inhibition.¹ Nitrofurantoin can only achieve therapeutic concentrations in the urine, therefore it is used only in urinary tract infections (UTIs) that are confined to the bladder (e.g. cystitis without systemic signs of infection/uncomplicated UTI). When using nitrofurantoin, what are some things to know?

What is nitrofurantoin's spectrum of activity?

Nitrofurantoin has activity against some Enterobacterales (e.g. *E. coli*, *Klebsiella* spp.), *Staphylococcus* spp., and *Enterococcus* spp. The following are intrinsically resistant: *Proteus* spp., *Serratia* spp., *Morganella* spp., *Providencia* spp., and *Pseudomonas* spp.^{1,2} Since it is not a β -lactam, it is unaffected by [ESBLs](#) and can be used to spare carbapenems in cystitis if susceptible.

What are toxicities of nitrofurantoin?

A review of controlled trials for treatment of UTIs showed toxicities associated with nitrofurantoin were infrequent, mild, and primarily gastrointestinal.³ Aside from GI adverse events, nitrofurantoin can cause acute or chronic pulmonary fibrosis, liver toxicity, peripheral neuropathy, and hemolytic anemia.^{1,2} It is generally considered [low risk for *C. difficile* infection](#).

When should nitrofurantoin be avoided in patients with renal impairment?

When originally approved in 1953, use was contraindicated in those with a creatinine clearance < 40 mL/min, but was updated in 2003 to reflect the new threshold of 60 mL/min. Rationale for this change is unclear, and evidence has suggested that a threshold of < 30 mL/min is safe and efficacious and supported by the American Geriatrics Society.⁴⁻⁶

Key takeaway: Nitrofurantoin is a preferred option for the management of UTIs confined to the bladder (i.e. cystitis) because it has high likelihood of activity against the most common urinary pathogen, is well tolerated, and has a low risk for *C. difficile* infection. Its use can preserve the use of other broader or more toxic alternatives (e.g. fluoroquinolones). It should be avoided in patients with creatinine clearance < 30 mL/min.

References:

1. Horton JM, Drekonja DM. Urinary Tract Agents: Nitrofurantoin, Fosfomycin, and Methenamine. In: Bennett JE, Dolin R, Blaser MJ, ed. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*. 10th ed. Philadelphia, PA: Elsevier; 2026:481-486.e2.
2. Macrobid (nitrofurantoin) [Package Insert]. Procter & Gamble Pharmaceuticals, Inc., Cincinnati, OH; 2009.
3. Huttner A, Verhaegh EM, Harbarth S, Muller AE, Theuretzbacher U, Mouton JW. Nitrofurantoin revisited: a systematic review and meta-analysis of controlled trials. *J Antimicrob Chemother*. 2015; 70(9):2456-64. doi: 10.1093/jac/dkv147.
4. Oplinger M, Andrews CO. Nitrofurantoin contraindication in patients with a creatinine clearance below 60 mL/min: looking for evidence. *Ann Pharmacother*. 2013; 47:106-111. doi: 10.1345/aph.1R352.
5. Geerts AFJ, Eppenga WL, Heerdink R, et al. Ineffectiveness and adverse events of nitrofurantoin in women with urinary tract infection and renal impairment in primary care. *Eur J Clin Pharmacol*. 2013; 69:1701-1707. doi: 10.1007/s00228-013-1520-x.
6. The American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatric Society 2015 updated Beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2015; 63(11):2227-46. doi: 10.1111/jgs.13702.