



Clinical Pharmacology & Toxicology Pearl of the Week

Nitrofurantoin - Part 1

- ✓ Nitrofurantoin (Macrobid) is a nitrofuran antimicrobial that is commonly used to treat uncomplicated urinary tract infections in women.
- ✓ It has a unique mechanism of action:
 - The parent drug is taken up and reduced by bacterial proteins into reactive intermediates that inactivate or alter bacterial ribosomes, leading to inhibition of protein synthesis, aerobic metabolism, DNA, RNA and cell wall synthesis.
- ✓ Nitrofurantoin has a broad spectrum of activity, with minimal bacterial resistance due to its multi-modal mechanisms of action.
- ✓ Nitrofurantoin is bactericidal in the urine at therapeutic doses, however is ineffective at treating any other type of infection as it concentrates in the urine only.
- ✓ It is indicated for use in patients with a creatinine clearance of >60 mL/minute, and therefore should not be used in those with renal impairment.

Nitrofurantoin pharmacokinetics:

- Good oral bioavailability (60-90%), especially when taken with food (food increases absorption by up to 40%)
- Nitrofurantoin has a $V_d = 0.8L/kg$, which is moderate
- Up to 60% of the drug is metabolized into inactive metabolites by body tissues (no CYP interactions)
- The drug and its metabolites are excreted, and therefore concentrated, in the urine.
- Nitrofurantoin has a half-life of 20-60 minutes depending on formulation
- ✓ Nitrofurantoin has been associated with numerous serious adverse effects, including:
 - Bacterial superinfection (C. Diff colitis, although this is a low risk drug for this)
 - Hemolysis in those with G6PD-deficiency
 - Peripheral neuropathy
 - Acute hepatitis (hepatocellular with a hypersensitivity-type reaction &/or cholestatic jaundice)
 - Pulmonary toxicity -
 - Acute pneumonitis
 - Subacute lung disease
 - Chronic interstitial lung disease (with chronic use)
- ✓ Stay tuned for Part 2, which discusses these Nitrofurantoin Toxicities!



The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 9am-5pm. The on-call physician is listed in ROCA. Click [HERE](#) for clinical issues the CP service can assist with.



The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414, and select option 1.

References:

1. Lexicomp (2019): Lexi-Drugs Nitrofurantoin
2. CMAJ June 16, 2015 187 (9) 648-656; DOI: <https://doi.org/10.1503/cmaj.150067>