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Title: Cystitis Treatment with Nitrofurantoin

Introduction

1. Urinary tract infections (UTI) affect 150 million each year, with 50-60% of women developing at least one UTI in their lifetime.
2. Costs of these infections, ranging from societal to health care costs, are approximately $3.5 billion per year in the US alone.
3. Most commonly caused by *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Enterococcus faecalis.*
4. Inadequate treatment can lead to recurring symptoms, disseminating infections, and increasing bacterial resistance.

Pharmacology	
Mechanism of Action	Inactivation in bacterial ribosomal protein→inhibition of protein, DNA/RNA and cell wall synthesis

Dose	• Acute uncomplicated cystitis
	  ○ Macrobid®: 100 mg twice daily ← **On Grady formulary**
	  ○ Macrodantin®: 50-100mg every six hours
	  ○ Duration: 5 days for women, 7 days for men
	• Cystitis Prophylaxis
	  ○ Macrobid®: 100mg once daily at bedtime
	  ○ Macrodantin®: 50-100mg once daily at bedtime
	  ○ Duration: 3-12 months – prolonged use has been associated with increased side effects

Susceptible bacteria	• E. Coli, Klebsiella, Enterococcus (including VRE), Staphylococcus Saprophyticus, Enterobacter
Formulation	Nitrofurantoin 100mg capsule: ~$2-6 Nitrofurantoin suspension 25mg/5mL, 10mg/mL (per mL): ~$3
PK/PD	**Does not reach therapeutic levels in serum or kidneys. Only concentrated in urine.** **Taking with food increases absorption by 40%**
Adverse Effects	• Peripheral neuropathy, pulmonary toxicity (extended use) • Hepatic dysfunction, superinfection (C. Difficile), hemolytic anemia (caution if G6PD deficient)
Interactions and warnings	• **Avoid use in CrCl < 30mL/min (decreased efficacy and increased risk of side effects)** • Contraindicated in children < 1 month (risk of hemolytic anemia)

Pregnancy	• **Contraindicated in pregnant patients at term (38-42 weeks gestation), during labor/delivery**
	  ○ Increased risk of hemolytic anemia and jaundice developing in neonate
	• **Indicated for asymptomatic bacteriuria in pregnant patients during first trimester**
	  ○ Macrobid®: 100mg twice daily x 4-7 days
	  ○ Use if other antibiotics are contraindicated or cannot be utilized
	  ○ Consider alternative if pregnant patient has a G6PD deficiency

Breastfeeding	• **Avoid in:**
	  ○ Breastfeeding patients with premature infants or < 1 month of age
	  ○ Breastfeeding patients with infants of any age if patient has G6PD deficiency
	• **Can consider:**
	  ○ Breastfeeding patients with full-term infants > 1 month of age

Comments	**Do not use for indication other than cystitis (pyelonephritis, prostatitis, bacteremia etc.)** **Commonly resistant organisms: Proteus, Pseudomonas**

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Overview of Evidence			
Author, year	Design/ sample size	Intervention & Comparison	Outcome
Christiaens TC, 2002	Prospective RCT- placebo controlled (n = 78)	Nitrofurantoin 100mg QID vs placebo x 3 days in females with uncomplicated UTI w/ pyuria	Combined sx improvement and cure for Nitrofurantoin Day 3: 27/35 (p = 0.08) Day 7: 30/34 (p= 0.003) **Nitrofurantoin achieved higher rate of bacteriologic cure and symptomatic relief compared to placebo**
Gupta K, 2007	Prospective open label RCT (n = 338)	Nitrofurantoin 100mg BID x 3 days vs Bactrim 1 DS tab BID x 3 days	Clinical Cure: Nitrofurantoin 84% vs. Bactrim 79% (not significant) Microbiological cure on day 3 of nitrofurantoin achieved in 127/130 (98%) of patients **Nitrofurantoin x 5 days = Bactrim x 3 days clinically and microbiologically**
Irvani A et al. 1999	Prospective double blind RCT (n = 521)	Cipro 100mg BID x 3 days Nitrofurantoin 100mg BID x 7 days Co-trimoxazole DS BID x 7 days	**Clinical resolution** 4- 10 days after therapy and at the 4- 6 week follow-up **was similar among the three treatment groups.** *(of note, normal dosing with Cipro is 500mg daily x3 days)*
Ingalsbe ML, 2015	Retrospective chart review	Macrobid 100mg BID Macrodantin 50-100mg QID Treated for 5-14 days Safety and clinical cure **in males with UTIs** and catheter-associated UTIs	A CrCl of $\geq$ 60 ml/min is suggested for men to achieve an 80% cure rate for most UTIs **Cure rate with specific organisms varied with CrCl but adverse events did not**

Conclusions

- Nitrofurantoin is a first line recommendation per IDSA for treatment of acute uncomplicated cystitis.
- Most studies have demonstrated a clinical cure rate with nitrofurantoin of 88%-93% and a bacterial cure rate of 81% - 92%.
- With high rates of efficacy, low risk of resistance, and lack of side effects, nitrofurantoin is an optimal first line agent for cystitis.
- Due to the lack of therapeutic concentration outside of the urine, nitrofurantoin is not recommended for pyelonephritis, urosepsis, or prostatitis.

References

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