

NITROFURANTOIN



In this column, Sharon Rees aims to refresh knowledge and interest in some of the commonly used drugs in a series of tweets. This month she is talking about **#nitrofurantoin**



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Day 1: **#nitrofurantoin** was licensed as an oral antibiotic for urinary tract infections (UTIs) in the 1950s and it is notable for still being in first line use with little antimicrobial resistance. In the 1970s, trimethoprim (TMP) became more popular, but resistance issues (28% of E.coli is resistance to TMP in UK) led to resurgent popularity



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Day 2: **#nitrofurantoin** is a broad spectrum antibiotic for uropathogens, with high cure rates equivalent to trimethoprim. Extended spectrum beta lactamase producing E.coli & Klebsiella are still sensitive to **#nitrofurantoin**, hence used as second line treatment in primary care. Effective as a three day course for uncomplicated UTI in healthy women, dose 100 mg modified release twice/day; also used at 50 mg four times/day for five days



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Day 3: Unusual kinetics for **#nitrofurantoin** mean it is used as a treatment for UTIs only. Rapid oral absorption and 60-75% undergoes first pass metabolism. The remainder is highly soluble. It concentrates in renal/urinary tissue as unchanged drug for elimination, where it can kill the bacteria. The $t_{1/2}$ is ~30 mins. Macrobid forms a gel in GI tract allowing slow release and twice daily dosing.



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Day 4: Bacterial nitroreductases transform **#nitrofurantoin** into a reactive entity which inflicts multiple system attacks on RNA, DNA, proteins & inhibits the citric acid cycle. Its



action is confined to the urinary tract with negligible tissue penetration elsewhere; this prevents carcinogenic risk to other tissues re the drug mechanism of action (DNA damage)

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Day 5: **#nitrofurantoin** was in clinical use predating regulation standards, so much information is unknown about adverse drug reactions! ADRs include brown urine, abdominal pain, blood disorders such as agranulocytosis, peripheral neuropathy. Psychiatric effects can occur but unknown frequency. Pulmonary fibrosis has been associated with long-term use (months/years); list not exhaustive



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Day 6: Drug-drug interactions are mostly moderate relating to an increased risk of peripheral neuropathy such as isoniazid, amiodarone, metronidazole; Severe DDIs with dapsone and prilocaine causing methaemoglobinaemia. **#nitrofurantoin**'s action is antagonised by quinolones and there is reduced absorption if antacids/foods delay gastric emptying. Inactivates the typhoid vaccine (not exhaustive)



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Day 7: Low resistance to **#nitrofurantoin** is thought to be because of the multiple attacks on bacterial structures - bacteria find it difficult to overcome more than one line of attack and survive to pass on several resistance mutations. This scenario is improbable in one organism

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In addition to the tweets, read the BNF section on 'urinary tract infections' and the monograph on nitrofurantoin. Another useful source is the Summary of Product Characteristics for nitrofurantoin. Please submit the answers to reesprescribe@gmail.com as a numbered list with TRUE/FALSE or the correct A,B,C,D option. If you achieve 8 or more out of ten on the questions, a CPD certificate will be emailed to you.

Further reading on #mercaptapurine

- **Nitrofurantoin 50mg Tablets:**
<https://medicines.org.uk/emc/product/3601/smpc#gref>
- **Macrobid Capsules 100mg B.P.:**
<https://www.medicines.org.uk/emc/product/429/smpc#gref>

Electronic Medicines Compendium. Macrobid Capsules 100mg B.P. <https://www.medicines.org.uk/emc/product/429/smpc#gref> (accessed 18 September 2020)

Electronic Medicines Compendium. Nitrofurantoin 50 mg Tablets. 2020. <https://www.medicines.org.uk/emc/product/3601/smpc#gref> (accessed 18 September 2020)

- 1 Nitrofurantoin was discovered in the 1960s
TRUE or **FALSE**?
- 2 Many adverse drug events are poorly classified for this drug because it was developed before rigorous research was required
TRUE or **FALSE**?
- 3 Nitrofurantoin is narrow spectrum because it only works on the urinary tract
TRUE or **FALSE**?
- 4 Nitrofurantoin has unusual kinetics because
 - A. It has very low levels of first pass metabolism
 - B. It has a very long half-life
 - C. High levels of unchanged drug accumulate in the urinary tract
 - D. It is a prodrug and needs high levels of functioning liver enzymes to work
- 5 Nitrofurantoin has higher antimicrobial resistance compared to trimethoprim
TRUE or **FALSE**?
- 6 The mechanism of action for nitrofurantoin is best described as
 - A. A multi-pronged attack on nucleic acids and protein
 - B. A prolonged attack on cell mitochondria
 - C. Hydrolysis of the bacterial cell membrane
 - D. Impairs manufacture of peptidoglycan
- 7 Nitrofurantoin is bacteriostatic
TRUE or **FALSE**?
- 8 Which of the following is **TRUE**?
 - A. Nitrofurantoin can cause brown or yellow urine
 - B. Nitrofurantoin has multiple severe drug-drug interactions
 - C. Nitrofurantoin precipitates in the urine making it highly concentrated
 - D. Nitrofurantoin can be used at all levels of eGFR
- 9 Nitrofurantoin is thought to have low levels of anti-microbial resistance because despite its age, it has not been used a lot around the world
TRUE or **FALSE**?
- 10 Nitrofurantoin is safe to use in all age groups
TRUE or **FALSE**?