

# Best Practice Message

June 2023

## Urinary Tract Infection management

### **Practice changing moments**

- Prescribe nitrofurantoin by brand to ensure correct formulation is prescribed (modified release capsules vs immediate release tablets).
- The risk of pulmonary and hepatic effects increases with longer treatment nitrofurantoin durations. Consider if alternative non-antibiotic prophylaxis agents may be appropriate.
- Due to the risk of treatment failure and adverse effects, nitrofurantoin should not be used in a patient with a Creatinine Clearance <60mL/min unless under specialist advice.
- Urinary alkalisers such as Ural® may affect nitrofurantoin and may be ineffective. Consider alternative symptom benefit if required.

### **Introduction**

Use of nitrofurantoin has increased in recent years due to increasing resistance to trimethoprim. It has overtaken trimethoprim for the treatment of Urinary Tract Infections (UTIs) since mid 2021 and has continued to rise in use. This coincided with the funding of the Macrobid® modified release capsules which allow for a twice daily dosing regimen. Pharmacist directed treatment of UTIs was also updated to allow for the supply of nitrofurantoin to women with an uncomplicated UTI since November 2022, further increasing the utilisation of nitrofurantoin.

### **Prescribe by brand**

Since March 2021, nitrofurantoin has been available in two formulations, *Nifuran*® immediate release tablets (50mg and 100mg) and *Macrobid*® modified release capsules (100mg). The modified release formulation is preferred in most patients due to the twice daily dosing regimen compared to four times daily for the immediate release tablets. However the modified release formulation is only indicated for treatment dosing in patients aged 12 years and older<sup>1</sup>. It is important to prescribe by brand to prevent inadvertent over or under dosing due to incorrect formulation selection. Approximately one third of prescriptions of nitrofurantoin tablets dispensed in the first quarter of 2023 were for a quantity which suggests intention to treat with Macrobid® Capsules.

### **Checking kidney function**

It is estimated one third of patients aged 65 or older may have an eGFR of <60mL/min/1.73m<sup>2</sup><sup>11</sup>. 41% of prescriptions for nitrofurantoin in 2022 were prescribed to patients in this age group. Nitrofurantoin is recommended to only be used in patients with a Creatinine Clearance >60mL/min. Reduced renal impairment causes inadequate concentrations of drug to appropriately treat infections and can lead to an increased risk of adverse effects. However, more recently, this has been disputed<sup>12</sup>. In 2019 the Medicines Adverse Reactions Committee met to discuss recent findings about the renal function cut-off and voted to continue with the current criteria of >60mL/min as the appropriate cut-off for nitrofurantoin use<sup>13</sup>. Consider if alternative antibiotic treatment would be more appropriate in a patient with reduced renal function.

### **Nitrofurantoin induced toxicity and implications of treatment duration**

Nitrofurantoin has been implicated in both acute and chronic lung toxicity as well as hepatic toxicity. Acute lung toxicity is thought to occur as a hypersensitivity type reaction which on first presentation may take days to weeks to develop<sup>2</sup>. However, on repeat exposure the onset may occur within 24 hours<sup>3</sup>. Separately long term nitrofurantoin treatment can lead to long term pulmonary disease which may be irreversible<sup>4</sup>. Liver toxicity can also occur from short term and long term treatment, however risk is much higher with long term treatment<sup>5</sup>. Liver impairment generally resolves (slowly) after discontinuation however may be permanent<sup>6</sup>. If considering using nitrofurantoin for antimicrobial prophylaxis, patients should be monitored for Pulmonary and hepatic toxicity. Treatment should last no longer than 6 months<sup>7</sup>. Consider if non-antibiotic based prophylaxis may be more appropriate. Options have been discussed in a previous bulletin found [here](#).

### **Urinary Alkalisers and UTIs**

There has been some attention recently about the co-prescribing of nitrofurantoin and alkalisers. This is centred around the theoretical interaction that exists between the two products. The effectiveness of nitrofurantoin is greatest in an acidic urine environment. By increasing the urinary pH this may cause a reduction in efficacy<sup>8</sup>. However, this has not been directly studied in vivo and it remains to be seen if urinary alkalisers would reduce the efficacy of nitrofurantoin in a real patient. Evidence for the use of urinary alkalisers in the management of UTIs is poor. A recent Cochrane review could find no suitable papers to support the use of urinary alkalisers<sup>9</sup>. Previous research has also failed to show a relationship between urinary pH and cystitis symptoms<sup>10</sup>.

### Other reading:

[He Ako Hiringa - Nitrofurantoin first for lower urinary tract infections](#)

[Medsafe - Spotlight on Nitrofurantoin](#)

[Lower UTI in Women HealthPathway \(not yet localised\)](#)

### References:

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13. Update on Nitrofurantoin Use in Renal Impairment [Internet]. 2019 [cited 2023 May 16]. Available from: <https://www.medsafe.govt.nz/committees/marc/reports/177-3.2.4%20Update%20on%20nitrofurantoin%20use%20in%20renal%20impairment.pdf>

**Authored by:** Ben Firestone

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