Surrey Heartlands Integrated Care System (ICS) Area Prescribing Committee (APC)

Prescribing and Monitoring Guidance for Nitrofurantoin in Primary Care

This guidance is intended to support:

- Prescribing recommendations for urinary tract infection as part of the NICE/PHE Common Infections Guidance [1]
- Monitoring guidance as part of the Specialist Pharmacy Services (SPS) Drug Monitoring Guidance [2] : Recommendations for tests prior to starting treatment with nitrofurantoin (long-term) are included; however for ongoing monitoring (long-term/prophylaxis) the recommendations are that monitoring is recommended periodically but no specified frequency (please see below)

Nitrofurantoin- Key Prescribing Points:

- **Avoid concurrent use with over the counter (OTC) products for cystitis*:*** *OTC products containing potassium or sodium citrate salts relieve symptoms by making the acidic urine (resulting from the bacterial infection) more alkaline. However, urine alkalisation reduces the effect of nitrofurantoin*
- **Long-term/ prophylaxis: monitor renal function, liver function and pulmonary symptoms every 6 months (more frequent monitoring (3 months) should be considered for the elderly and/or where there are concerns about a patients clinical condition, concomitant drugs, or comorbidities)[3]** (also consider for repeated treatment courses): *monitor patients renal function, liver function and pulmonary symptoms* (consider measuring using symptom assessment and spirometry (if available)).*
- **Do not use for upper urinary tract infection (UUTI)*:*** *Nitrofurantoin only achieves antibiotic concentration in the urine with low circulating blood levels and poor tissue penetration making it unsuitable for the treatment of upper UTIs*
- **Poor Renal function- avoid if GFR < 45mls/min:** *Nitrofurantoin is preferentially excreted into the lower urinary tract (approx 30-40%). If eGFR < 30mls/min - therapeutic concentrations unlikely to be obtained and treatment failure likely. eGFR should preferably be ≥ 45mls/min. (if eGFR between 30-44mls/min use only if no other options and for short courses of 3-7 days)*
- **Pregnancy and lactation- avoid in pregnant women at term and avoid in breast feeding:** *Animal studies with nitrofurantoin have shown no teratogenic effects. However, it is contraindicated in infants < 3 months of age and in pregnant women during labour and delivery, due to possible risk of haemolysis of the infants' immature red cells. Breast feeding an infant known or suspected to have an erythrocyte enzyme deficiency (including G6PD deficiency), must be temporarily avoided, since nitrofurantoin is detected in trace amounts in breast milk*

***Pulmonary Symptoms:** Nitrofurantoin is one of the commonest causes (although relatively rare) of drug induced pulmonary disease/toxicity, which can potentially be serious and even fatal. Pulmonary toxicity can be either acute or chronic.

Acute pulmonary reactions usually occur within the first week of treatment and are reversible when treatment is stopped. Acute symptoms include: fever, chills, cough, chest pain, breathlessness, and chest x-ray abnormalities.

Interstitial Pulmonary fibrosis (IPF) is a rare condition and can be associated with the use of nitrofurantoin. If pulmonary toxicity is suspected / detected nitrofurantoin should be stopped immediately. Chronic pulmonary reactions (including IPF) can develop insidiously and can

include mild fever, chills, persistent cough, breathlessness, tiredness and clubbing of the fingers. If pulmonary symptoms are not detected early and allowed to progress, this can become irreversible and, in some cases, fatal. Monitoring of pulmonary symptoms for patients on long-term prophylaxis is therefore very important and should be checked at least every 6 months (see above).

Patients should also be advised to report any symptoms suggestive of pulmonary toxicity, such as cough, chest pain and shortness of breath.

Regular review of the continued requirement for prophylaxis is also important particularly in the elderly.

British National Formulary (BNF) advice is to discontinue if there is a deterioration in lung function for patients on long-term therapy.

References:

1) NICE/PHE Common Infections Guidance: https://www.bnf.org/wp-content/uploads/2021/07/summary-antimicrobial-prescribing-guidance_july-21-for-BNF.pdf
2) Specialist Pharmacy Services (SPS) : Suggestions for Drug Monitoring of Adults in Primary Care Guidance: https://www.sps.nhs.uk/home/guidance/drug-monitoring/ [accessed 6.9.21]
3) Local agreement on frequency for ongoing monitoring by the Surrey Heartlands Antimicrobial Stewardship (AMS) Collaborative Working Group June 2020
4) British Lung Foundation (BLF) : Pulmonary Fibrosis: https://www.blf.org.uk/support-for-you/pulmonary-fibrosis/symptoms
5) British National Formulary (BNF) : https://bnf.nice.org.uk/drug/nitrofurantoin.html [Accessed 24.5.21]
6) Electronic Medicines Compendium (eMC): https://www.medicines.org.uk/emc/
7) Madani, Y., Mann, B. Nitrofurantoin-induced lung disease and prophylaxis of urinary tract infections. *Prim Care Respir J* **21,** 337–341 (2012). https://doi.org/10.4104/pcrj.2012.00059