Long-term nitrofurantoin safety monitoring guidance

This guidance has been produced following two serious patient safety events involving long-term nitrofurantoin treatment. One patient is now terminally ill with pulmonary fibrosis and the other patient suffered jaundice as a result of long-term treatment.

Guidance on long-term nitrofurantoin use:

- Our local antibiotic prescribing guidance recommends:
  - Nitrofurantoin can be used for long-term low dose prophylaxis of recurrent UTIs, taken at bedtime.
  - A 6-month trial is recommended as this reflects the duration of most trials of prophylactic antibiotics and information on long-term follow-up is lacking.

Monitoring requirements for patients who are prescribed long-term nitrofurantoin:

- Spirometry should be carried out every 3-6 months
- Liver Function Tests (LFTs) should be checked every 3-6 months
- Renal function should be checked every 3-6 months

Action required:

1. A search identifying patients who are prescribed nitrofurantoin on repeat can be found in ‘Enterprise Search and Reports’ – go to the Medicines Management folder, open the ‘2016’ folder and you will find a search called ‘Nitrofurantoin- patients on long-term treatment’.
2. Confirm that the patient identified is on long-term treatment
3. Identify those who have not had liver function, lung function and/or renal function checked in the last 6 months or those with results outside normal limits.
4. Identify those who have reported signs or symptoms of peripheral neuropathy.
5. Review patients who have not had the recommended monitoring and ensure that it is undertaken as soon as possible.
6. Put in place a recall process for future monitoring if nitrofurantoin needs to continue.
7. Ensure practice nurses are aware of the reasons for spirometry and that recall is needed even when recurrent results show no pulmonary effects.

Background information

Pulmonary toxicity

- It is well documented that although rare, nitrofurantoin can cause pulmonary toxicity acutely, sub-acutely and chronically.
- If pulmonary toxicity is suspected/detected nitrofurantoin should be stopped immediately
- Acute pulmonary reactions usually occur within the first week of treatment and are reversible on cessation of therapy. Acute pulmonary reactions are commonly manifested by fever, chills, cough, chest pain, dyspnoea, pulmonary infiltration with consolidation or pleural effusion on chest x-ray and eosinophilia.
- In sub-acute pulmonary reactions, fever and eosinophilia occur less often than in the acute form.
- Chronic pulmonary reactions (including pulmonary fibrosis and interstitial lung disease) can develop insidiously, and may occur more commonly in elderly patients. Minor symptoms such as fever, chills, cough and dyspnoea may be significant. The severity of chronic pulmonary reactions and their degree of resolution appear to be related to the duration of therapy after the first clinical signs appear. It is important to recognise symptoms as early as possible. Pulmonary function may be impaired permanently, even after cessation of therapy.

Patients receiving long-term nitrofurantoin should have lung-function checked, using spirometry, every 3-6 months.
Hepatic toxicity
- Hepatic reactions including cholestatic jaundice and chronic active hepatitis occur rarely, but fatalities have been reported.
- Cholestatic jaundice is generally associated with short-term therapy (usually up to 2 weeks). Chronic active hepatitis, occasionally leading to hepatic necrosis is generally associated with long-term therapy (usually after 6 months). The onset may be insidious. Treatment should be stopped at the first sign of hepatotoxicity.

Patients receiving long-term nitrofurantoin should have liver function checked every 3-6 months.

Renal impairment
- Nitrofurantoin is contraindicated in patients suffering from renal impairment with an eGFR < 45 ml/minute, although it may be used with caution as short-course therapy only for the treatment of uncomplicated lower urinary tract infection in individual cases with an eGFR between 30-44 ml/min to treat resistant pathogens, when the benefits are expected to outweigh the risks.

Patients receiving long-term nitrofurantoin should have renal function checked every 3-6 months.

Neurological toxicity
- Peripheral neuropathy (including optical neuritis) with symptoms of sensory as well as motor involvement, which may become severe or irreversible have been reported
- Treatment should be stopped at the first sign of neurological involvement.

Further monitoring guidance can be obtained from the Summary of Product Characteristics. Access via: www.medicines.org.uk

Reporting Medication Safety Incidents
Please continue to report any medication safety incidents as they provide valuable learning for all healthcare professionals. These can be reported by phone, email, Significant Event Form or via Datix to the CCG’s Medicines Management Team – 01952 580436, Sharon.reece@nhs.net