PostScriptPrimaryCare

NHS Greater Glasgow and Clyde

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This edition contains articles on:

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- Codeine: restricted analgesic use in children and adolescents
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Diclofenac: new contraindications and warnings after review of cardiovascular safety

The MHRA has issued updated advice for diclofenac after a Europe-wide review found further evidence that the arterial thrombotic risk with diclofenac is similar to that for COX-2 inhibitors.

The new treatment advice applies only to systemic formulations (ie tablets, capsules, suppositories, and injections) of diclofenac.

Advice for healthcare professionals:

New advice for diclofenac

- Diclofenac is now contraindicated in patients with established:
  - ischaemic heart disease
  - peripheral arterial disease
  - cerebrovascular disease
  - congestive heart failure (NYHA classification II–IV)

  Patients with these conditions should be switched to an alternative treatment at their next routine appointment
- Diclofenac treatment should only be initiated after careful consideration for patients with significant risk factors for cardiovascular events (eg hypertension, hyperlipidaemia, diabetes mellitus, smoking)

Reminder of existing advice for all NSAIDs

- The decision to prescribe an NSAID should be based on an assessment of a patient's individual risk factors, including any history of cardiovascular and gastrointestinal illness
- **Naproxen** and **low-dose ibuprofen** are considered to have the most favourable thrombotic cardiovascular safety profiles of all non-selective NSAIDs
- The lowest effective dose should be used for the shortest duration necessary to control symptoms. A patient's need for symptomatic relief and response to treatment should be re-evaluated periodically

Codeine: restricted analgesic use in children and adolescents

The MHRA has issued a Drug Safety Update covering new restrictions on the use of codeine for analgesia in children and adolescents under 18years following a European safety review. The review was triggered by case reports of children who received codeine for pain control after tonsillectomy or adenoidectomy (or both) for obstructive sleep apnoea and who developed rare, but life-threatening adverse events, including death.

Codeine is converted to morphine in the liver by the CYP2D6 enzyme. There are many genetic variations of *CYP2D6*, which affect the extent of this conversion in individuals. Different plasma morphine concentrations in patients' blood leads not only to different levels of pain relief, but also to a variable and unpredictable risk of side effects due to morphine's action on the brain and respiratory centre.

MHRA advice for healthcare professionals:

- Codeine should only be used to relieve acute moderate pain in children older than 12 years and only if it cannot be relieved by other painkillers such as paracetamol or ibuprofen alone
- Codeine is now contraindicated in:
  - all children age 0–18 years who undergo tonsillectomy or adenoidectomy (or both) for obstructive sleep apnoea
  - all patients of any age known to be CYP2D6 ultra-rapid metabolisers
- Codeine is not recommended for use in children whose breathing might be compromised, including those with neuromuscular disorders, severe cardiac or respiratory conditions, upper respiratory or lung infections, multiple trauma, or extensive surgical procedures. Morphine toxicity may be increased in these settings
- In children age 12–18 years, the maximum daily dose should not exceed 240 mg. This may be taken

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in divided doses up to four times a day at intervals of no less than 6 hours. It should be used at the lowest effective dose for the shortest period. Duration of treatment should be limited to 3 days and if no effective pain relief is achieved, treatment should be reviewed by a physician
- Information should be given to parents and caregivers on how to recognise the signs and symptoms of morphine toxicity, and advice should be given to stop giving the child codeine and to seek medical attention immediately if the child shows these signs or symptoms, which include reduced levels of consciousness, somnolence, respiratory depression, 'pin-point' pupils, lack of appetite, constipation or nausea and vomiting
- Codeine should not be used by breastfeeding mothers because it can pass to the baby through breast milk and potentially cause harm

Ticagrelor and simvastatin

As mentioned in Postscript 75 (May 2013), ticagrelor (Brilique®) has been added to the NHSGGC Adult Formulary for patients with troponin positive acute coronary syndromes (defined as non-ST elevation myocardial infarction [NSTEMI] or ST elevation myocardial infarction [STEMI]).

There is an interaction between ticagrelor and simvastatin where ticagrelor may increase the exposure to simvastatin increasing the risk of adverse effects. This is only clinically significant at simvastatin doses **exceeding 40mg** which are no longer recommended and all patients on these high doses should be reviewed.

Also of note, the metabolism of ticagrelor is inhibited by clarithromycin and other potent CYP3A4 inhibitors. These drugs should be avoided during ticagrelor treatment or the patient switched to clopidogrel.

Spiriva Respimat® removed from Formulary

The MHRA has previously reported potential cardiac adverse effects with this inhaler device and a 2012 meta-analysis indicated that it was associated with a universally increased risk of overall death compared with placebo, Spiriva HandiHaler®, long-acting $beta_2$ agonists and long-acting $beta_2$ agonists plus inhaled corticosteroids in combination.

The risk of cardiovascular death was greater in patients with severe COPD and at higher dose. The product was removed from the NHSGGC Formulary in June 2013 but has not been withdrawn by the manufacturer.
Recommendations for prescribers:

- All patients currently prescribed Spiriva (tiotropium) Respimat® be identified and reviewed at the next available opportunity
- As part of review, the patient's overall condition should be taken into account, eg cardiovascular risk factors as well as response to treatment
- Alternative treatment should be considered in at risk patients. Other options include long-acting $beta_2$ agonists, Spiriva Handihaler® or, where appropriate, ICS/LABA combination inhaler
- Report all suspected tiotropium adverse reactions via the Yellow Card reporting scheme

Primary Care Antimicrobial Guidelines Prescribing app

'GP Antibiotics' is a simple, searchable, pocket reference for the current NHSGGC adult and paediatric antimicrobial guidelines. It has a clean modern user interface, and is free to download from the Apple App Store or Android Google Play Store.

The app is intended to support the prescribing of antimicrobials in the community and prescribers should find it particularly useful when undertaking house calls or care home visits. For more information on the app, including screenshots and a video outlining the features, please visit Polwarth Limited.

Vedagrin herbal product

The MHRA has instructed the manufacturers of Vedagrin (also know as Vedanate) to stop selling the product after making false claims. The unlicensed herbal medicine was promoted as an alternative to prescribed diabetes medication with the words 'say goodbye to your diabetes medication forever' which breaks advertising regulations for medicines and should be ignored.

It is important that people only buy herbal medicines with either a PL (Product Licence) or THR (Traditional Herbal Registration) number on the packaging. This means the medicines have been assessed against quality standards.

Primary Care clinical guidelines

The following primary care guidelines have been posted on the Clinical Guideline Electronic Resource Directory:
- Antiplatelet therapy in the secondary prevention of coronary heart disease
- Guidance for the review of patients (with or without DXA) treated with oral bisphosphonates for fracture risk reduction

Click **HERE** for the full list of June additions.

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