PostScript

NHS Greater Glasgow and Clyde

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This edition contains articles on:

Safety update

Antiepileptic drugs (AEDs)

The MHRA issued advice in November 2013 on the appropriateness of generic prescribing of AEDs and when a patient should stay on a particular brand. This initial guidance is directed at all staff across NHSGGC involved in the prescribing, supply and administration of medicines prescribed for the treatment of epilepsy. The need for more detailed guidance is being considered. This advice is only for the management of epilepsy. Patients on AEDs for neuropathic pain do not require specific brand / manufacturer prescribing.

Phenytoin, carbamazepine, phenobarbital, primidone

Prescribers should ensure that their patient is maintained on a specific preparation.

All other AEDs being used to treat epilepsy

Though many patients diagnosed with epilepsy will already be maintained on a single brand or formulation, some of these patients will have historically been prescribed medicines generically and will have previously been subject to variance on the manufacturer of the generic preparation supplied.

For levetiracetam, lacosamide, tiagabine, gabapentin, pregabalin, ethosuximide and vigabatrin, it is not necessary to ensure that patients are maintained on a specific product unless there are risks in doing so.

Patients prescribed valproate, lamotrigine, perampanel, retigabine, rufinamide, clobazam, clonazepam, oxcarbazepine, eslicarbazepine, zonisamide or topiramate are not required to be maintained on a specific preparation. The prescriber may consider, following discussion at the patient's next review, that the circumstances require the need for continuity of supply, eg seizure risk.

How to maintain patients on a specific brand or manufacturer's preparation

- All sectors of care should prescribe and dispense by brand name where it is possible.
- For those medicines that are only available as generic medicines, continuity can be managed by detailing the manufacturer of the generic medicine in the prescription.
- For GP10 prescriptions, some prescribing systems will allow the choice of a particular manufacturer for a generic medicine. Where this is not possible, the generic manufacturer can be included in the dosing information so that the information is clear both to the pharmacy supplying the medicine and when the patient moves between sectors of care.
- Liaise with the patient to ensure that they are aware of the need to continue to use the same brand or manufacturer preparation.
- Liaise with the pharmacy supplying the medicine to ensure continuity of supply of a particular brand or manufacturer preparation.

Advice for patients admitted to hospital

- Check the Emergency Care Summary and at least one other information source, to determine if the patient's AEDs are prescribed using a specific manufacturer's product. If so, transcribe this information onto the Kardex.
- AEDs prescribed generically can be prescribed generically on the Kardex. The exceptions are phenytoin, carbamazepine, phenobarbital and primidone, which must be prescribed using a specific brand or manufacturer's preparation. Document decisions in the medicines reconciliation process.

Good practice points

- As it will take time to implement the MHRA advice, there will be patients admitted to hospital with AEDs prescribed generically but with risk factors requiring a change to one product. In such cases, it would be good practice to prescribe by brand where possible.
- Where a particular product is not available, consider the risks and benefits of a switch. Consider using a suitable alternative generic or brand of the same medicine.

Oxycodone Product of Choice

Several branded generic preparations of modified release (MR) oxycodone are now available. Longtec® was awarded the NHS Scotland acute care national contract and is the NHSGGC brand of choice. It will be supplied in the acute sector from January 2014. NHSGGC policy is that MR controlled drugs should be prescribed by brand name to minimise confusion and ensure consistency of supply across primary and secondary care.

Key points

- Morphine remains the preferred choice of strong opioid
- Oxycodone is restricted for use in patients when morphine is ineffective or not tolerated.
- Modified release oxycodone should be prescribed as Longtec® tablets.
- Immediate release oxycodone capsules or liquid should be prescribed generically. Any brand may be supplied.
- GP practices and community pharmacies started implementing this switch during December.
- Palliative care teams have been made aware of this change.
- Patients admitted to hospital on Oxycontin® can be safely switched to Longtec®.

Smoking cessation

Smoking cessation with or without pharmacotherapy has been associated with exacerbations of underlying psychiatric illness, eg depression, anxiety. The Smokefree smoking cessation service has received several enquiries about varenicline being prescribed to patients with a history of depression or currently being prescribed an antidepressant. Although a history of depression or active treatment with an antidepressant is not a contra-indication for varenicline use; varenicline should be used with caution in these circumstances.

The BNF advises, as per MHRA advice, that patients should discontinue treatment with varenicline and seek prompt medical advice if they develop agitation, depressed mood or suicidal thoughts and those with a history of psychiatric illness should be monitored while taking varenicline.

Safety update

Nitrofurantoin

As we highlighted in September, the MHRA have issued a reminder on precautions for use of nitrofurantoin in renal impairment, following a small number of reports of treatment failure in a single UK centre. In NHSGGC, as in much of the UK, this agent is recommended for lower urinary tract infections in patients without sepsis. Nitrofurantoin concentrates in the urine and has an excellent spectrum of activity against the majority of microbes causing UTI. In patients with renal impairment, secretion is reduced and this may result in treatment failure.

The SPC and MHRA state nitrofurantoin is contraindicated where creatinine clearance < 60ml/min. Advice in *GGC Therapeutics Handbook* is to avoid in patients with eGFR < 20ml/min/1.73m^2 and contact microbiology for an alternative.

The Antimicrobial Management Team is awaiting latest UK guidance from the soon to be updated *Renal Drug Handbook* before revising local guidance. At present prescribers should be aware of potential treatment failure with nitrofurantoin in those with reduced renal function. Prescribers should also be aware that alternative antibiotics in this population are associated with a significant increased risk of *Clostridium difficile* and also may have a narrower spectrum of activity against potential organisms causing UTI. These risks should be carefully considered and a measured judgment made for individual patients. **It is important to reiterate that asymptomatic bacteriuria is very common in the elderly and is absolutely not an indication for antibiotic therapy.**

There will be an update with definitive guidance following further consultation and publication of the *Renal Drug Handbook*.

Novel oral anticoagulants

The Heart MCN has proposed a strategy to offer prescribers a choice of novel oral anticoagulant (NOAC) or warfarin for patients newly diagnosed with non-valvular atrial fibrillation (AF) requiring anticoagulation. The clinical rationale is acknowledged, but such a strategy also has cumulative financial implications and requires consideration as part of the longer-term financial planning for NHSGGC.

The Board's Prescribing Management Group recommends that until the 2014/15 plan is agreed, the Formulary position for the NOACs is unchanged:

- NOACs are available for patients poorly controlled on warfarin (identified by GCAS, spending <60% time in therapeutic range) or warfarin allergy;
- NOACs remain non-Formulary for new patients
- Patients with a new AF diagnosis who require anticoagulation should start warfarin unless contraindicated.

Updates to this advice will be communicated through future editions of *PostScript* as it becomes available. Supporting information for prescribing these medicines will accompany letters from GCAS advising GPs of when a switch in anticoagulant treatment might be appropriate.

Antibiotic Interactions:

Quinolones and tetracyclines with metal salts and other cations

Quinolones, eg ciprofloxacin, levofloxacin, norfloxacin and ofloxacin; and tetracyclines, eg doxycycline, lymecycline and minocycline interact with products containing multivalent cations. Such products include:

- aluminium or magnesium-containing antacids
- multivitamins
- preparations containing calcium
- preparations containing iron
- preparations containing zinc
- sucralfate.

When oral quinolones or tetracyclines are given concomitantly with such products, there is often a significant reduction in the oral absorption of the antibiotic. The interaction is caused by formation of insoluble chelation complexes in the gastrointestinal tract that inhibit antibiotic absorption. This clinically significant interaction risks rendering the antibiotic ineffective. Serum antimicrobial levels can fall below minimum inhibitory concentration so becoming sub-therapeutic (particularly against organisms such as staphylococci and Pseudomonas aeruginosa) resulting in treatment failure. It has also been suggested that the low levels of antimicrobials which occur as a result of this interaction may contribute to the development of antimicrobial resistance.

A recent case involved an elderly male patient treated for an infective exacerbation of COPD with oral doxycycline. The patient's symptoms didn't improve within the first 24-48 hours of antibiotic therapy and escalation of empirical therapy was considered. However, it was also noted that the patient had been receiving concomitant ferrous fumarate. The iron was withheld and symptoms improved significantly over the next 24-48 hours without the need to escalate antimicrobial therapy.

Whenever possible, products containing multivalent cations should be avoided in patients receiving oral quinolones or tetracyclines. If both preparations are necessary, timing of administration may help minimise the effect. The BNF recommends that:

- Oral quinolones or tetracyclines should not be administered for at least 2 hours before or after indigestion remedies or medicines containing iron or zinc.
- When taking ciprofloxacin, norfloxacin and the older tetracyclines, milk and dairy products should be avoided 2 hours before and after oral drug administration.

Action for Prescribers and Pharmacists

- Be aware of the interaction between cations and quinolones / tetracycylines.
- Consider if the interacting cation, eg iron or antacid can be stopped for the duration of the antibiotic.
- If both products are required, ensure administration times are optimised to improve antibiotic absorption (see table below for advice from the SPCs).
- Follow NHSGGC antimicrobial guidelines, including recording of the duration of oral antibiotics.

Antibiotic	Co-administration with products containing magnesium, aluminium, iron, zinc, calcium or sucralfate	Co-administration with food and dairy products
Ciprofloxacin	• Potential 50-90% reduction in ciprofloxacin AUC (area under curve). • Administer at least 2 hrs before or after.	• Absorption not significantly affected by non-dairy foods. • Avoid milk, yoghurt, or calcium fortified orange juice 2 hours before or after.
Norfloxacin	• Potential 90% reduction in norfloxacin AUC. • Administer at least 2 hrs before or after.	• As above
Levofloxacin, ofloxacin	• Potential 20-40% reduction in antibiotic AUC. • Administer at least 2 hrs before or after.	• Absorption not significantly affected by food or dairy products.
Doxycycline, lymecycline, minocycline	• Potential 90-100% reduction in antibiotic AUC. • Administer at least 2 hrs before or after to improve antibiotic bioavailability.	• As above
Tetracycline, oxytetracycline	• Potential 90-100% reduction in antibiotic AUC. • Administer at least 2 hrs before or after to improve antibiotic bioavailability.	• Absorption affected by food and dairy products. • Avoid milk, yoghurt, or calcium fortified orange juice 2 hours before or after.

New NHSGGC guidelines

The following guidelines have been added to the repository on Staffnet

- Gluten Free Guidelines October 2013
- Primary Care Prescribing Guidelines for Oral Nutritional Supplements
- Unlicensed Medicine Protocol Prescribing Larvae
- Vitamin D Insufficiency Guideline
- Hypertension
- Cholesterol management

PostScript Extra Type 2 Diabetes

A new PostScript Extra bulletin on the **pharmacological management of adult patients with type 2 diabetes** is available here. This bulletin is an educational resource on the pharmacological management of type 2 diabetes. Appendix 1 provides a summary of pharmacology, licensed indications, and formulary status of antidiabetic medicines. See Appendix 2 for an overview of the different types of insulin, insulin devices and their Formulary status. Refer to the GGC Diabetes guideline for further details and information on how to manage individual patients.

ADTC decisions summary

See the website for full list of medicines and details of indications and restrictions.

Some additions to the *Adult Total Formulary*:

- **Atomoxetine (Strattera®)** for attention-deficit/hyperactivity disorder in adults as part of a comprehensive treatment programme restricted to specialist initiation.
- **Axitinib (Inlyta®)** for adult patients with advanced renal cell carcinoma after failure of prior treatment with sunitinib or a cytokine. Restricted to specialist use in accordance with regional protocol.
- **Enzalutamide (Xtandi®)** for adult men with metastatic castration-resistant prostate cancer whose disease has progressed on or after docetaxel therapy. Restricted to specialist use in accordance with regional protocol.
- **Mannitol inhaled (Bronchitol®)** for the treatment of cystic fibrosis (CF) in adults aged 18 years and above as an add-on therapy to best standard of care. Restricted to specialist initiation for patients who are not currently using dornase alfa due to lack of response, intolerance or ineligibility and have rapidly declining lung function and in whom other osmotic agents are considered unsuitable.
- **Vemurafenib (Zelboraf®)** as monotherapy for adult patients with BRAF V600 mutation-positive unresectable or metastatic melanoma. Restricted to specialist use for first-line treatment of BRAF V600 mutation-positive unresectable or metastatic melanoma pending regional protocol.

The following medicine was among those added to the *Paediatric Formulary*

- **Ondansetron** orodispersible films **(Setofilm®)** for chemotherapy-induced nausea and vomiting in children aged ≥6 months and prophylaxis and treatment of post-operative nausea and vomiting in children aged ≥4 years. Restricted to specialist initiation in patients with enhanced risk of aspiration or swallowing difficulties.

Nalmefene

We noted in the last edition that this new drug had been added to the Formulary for the for the reduction of alcohol consumption in adults with alcohol dependence who have a high drinking risk level, without physical withdrawal symptoms and who do not require immediate detoxification. Nalmefene should only be prescribed as part of a full care package including the provision of continuous psychosocial support by appropriate NHS personnel. Prescribers should consider whether a strategy of detoxification and abstinence may be more appropriate than the reduction approach offered by this medicine alongside a programme of psychosocial support.

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