TOWARDS SAFER USE OF ANTICOAGULANTS

Anticoagulants consistently appear in the ‘Top Ten’ medication incident reports for NHSGGC. There have been 73 incidents relating to warfarin reported and approved through Datix since April 2008, 34 involving heparin, 13 with enoxaparin and 8 with tinzaparin. Thank you to all staff who have reported medication incidents on Datix. The data is used to support improvements in the safe use of medicines throughout NHSGGC.

WARFARIN

Incident 1: A patient discharged on warfarin was given a supply of 1mg, 3mg and 5mg tablets labelled “one to be taken as directed by your doctor according to the INR”. The incident came to light when the GP was asked to visit weeks later because the patient had excessive bruising on her legs. The patient had been taking one tablet of each strength (9mg daily) resulting in an INR of 7.0. This had not been picked up sooner because the patient had not been referred to the NHSGGC Anticoagulant Service on discharge from hospital.

Incident 2: The Anticoagulant Service suggested that a GP consider whether warfarin therapy should be stopped and changed to aspirin, as the patient was at high risk of falls. The GP took this advice but did not tell either the community pharmacist or Anticoagulant Service. The community pharmacist continued to supply warfarin weekly in a dosette box against the original prescription, and the Anticoagulant Service continued to dose and monitor as it was unaware of the GP’s decision. The patient remained on both drugs until the Anticoagulant Service discovered the patient had a high INR and referred to the GP. The community pharmacist and Anticoagulant Service were informed so that no further warfarin was given.

Heparin

Incident 1: A patient was prescribed heparin as a bolus dose of 1000 units followed by 500 units per hour. This was prepared as 10000 units in 10ml therefore required a rate setting of 0.5ml/hour. The rate was set as 5ml/hour and so 10000 units were given over a two-hour period. The incident was identified when the alarm rang on the pump as the syringe had run out.

A similar incident involved the administration of heparin 1000 units/ml at a rate of 8ml/hour instead of 0.8ml/hour. On this occasion the error was noticed when a second nurse performed a regular check 30 minutes after the infusion had started.

Incident 2: A patient was given 25000 units heparin instead of 5000 units. This was as a result of a staff member selecting high strength heparin ampoules (5000 units/ml) instead of the more commonly used 1000 units/ml ampoules.

Learning points

• Discharge planning is essential for patients on anticoagulants, eg ensure an NHSGGC Anticoagulant Service appointment is arranged.
• Ensure labels on dispensed warfarin are clear AND that the patient understands them before discharge. Consider which strengths of warfarin should be prescribed and dispensed; practice varies across NHSGGC.
• Where several different groups are involved in care of the patient, effective communication between all parties is vital.

The National Patient Safety Agency (NPSA) also recognised the ongoing problem of significant and recurrent patient harm resulting from the inappropriate and incorrect use of anticoagulant therapy and released a Patient Safety Alert aimed at improving anticoagulant usage. NHSGGC has been working towards implementing these recommendations for some time via multidisciplinary working groups and has co-ordinated, and contributed to, many changes to date, such as:
• the introduction of a new and more detailed patient information booklet,
• rationalisation and standardisation of guidelines across NHSGGC,
• extension of the Anticoagulant Service to include Clyde hospitals,
• interaction with undergraduate schools to ensure that education programs are reviewed,
• development of an anticoagulant DOTs training package for junior medical staff,
• development of an updated NES training package for pharmacists,
• in-service training on safer anticoagulant management.

The Scottish Patient Safety Programme, referred to in PostScript 53, complements this work by focusing directly on the patient and the frontline staff to improve their knowledge, skills, awareness and management of the risks associated with anticoagulation.
Drugs

Agomelatine (Valdoxan®)  
Treatment of major depressive episodes in adults.  
Non-Formulary

Aprepitant (Emend®)  
Formulary appeal: prevention of acute and delayed nausea and vomiting associated with chemotherapy.  
Total Formulary: Restricted to use according to local protocol.

Bemiparin (Zibor®)  
Thromboprophylaxis in orthopaedic surgery.  
Non-Formulary

Droperidol (Xomolix®)  
Post-operative nausea and vomiting (PONV).  
Total Formulary: Restricted to use by consultant anaesthetists for use as a third-line antiemetic for PONV in patients with previous failure of other Formulary agents. The use of droperidol for addition to a PCA containing opiates remains non-Formulary.

Filgrastim (Ratiogranist®)  
Neutropenia/feltyte neutropenia.  
Total Formulary: Restricted to use in accordance with local protocol.

Imatinib tablets (Glivec®)  
Adjuvant treatment of adult patients following resection of Kit (CD117)-positive gastrointestinal stromal tumours (GIST).  
Non-Formulary

Liraglutide (Victoza®)  
Type 2 diabetes mellitus.  
Total Formulary: Restricted to third-line use.

Methylnaltrexone (Relistor®)  
Opioid-induced constipation in palliative care.  
Total Formulary: Restricted to use in accordance with regional protocol.

Nepafenac (Nevanac®)  
Prevention and treatment of post-operative pain and inflammation associated with cataract surgery.  
Non-Formulary

Pramipexole prolonged release (Mirapexin®)  
Parkinson’s disease.  
Total Formulary: Restricted to use on the advice of consultants with a special interest in Parkinson’s disease.

Prasugrel (Effient®)  
In combination with aspirin in patients with acute coronary syndrome undergoing primary or delayed percutaneous coronary intervention.  
Non-Formulary

Rifaxinam (MabThera®)  
Chronic lymphocytic leukaemia.  
Total Formulary: Restricted to use in accordance with regional protocol.

Tafelprost (Safilutan®)  
Open-angle glaucoma and ocular hypertension.  
Total Formulary: Restricted to patients with sensitivities to preservatives.

Thalidomide (Thalidomide Pharmion®)  
Multiple myeloma.  
Total Formulary: Restricted to use in accordance with regional protocol.

Valganciclovir (Valcyte®)  
Treatment of cytomegalovirus (CMV) retinitis in AIDS patients.  
Total Formulary: Restricted to use by HIV specialists and ophthalmologists specializing in ocular issues associated with HIV infection.

Valganciclovir (Valcyte®)  
Prevention of CMV disease in solid organ transplant patients.  
Total Formulary: Restricted to use by physicians experienced in the care of post-transplant patients.

Check our website http://www.glasgowformulary.scot.nhs.uk

Non-Formulary reporting in primary care

PostScript 47 (September 2008) highlighted the introduction of a non-Formulary (NF) monitoring policy for primary care. Introduction was phased through the CH(C)Ps and the roll-out was completed in February 2009. Between August 2008 and March 2009 156 NF forms were returned.

The number of forms returned per CH(C)P is shown in Table 1. It should be remembered that the order of roll-out will affect the number of completed forms in this time period. Adherence with the Preferred List ranged from 75% to 79% across the CH(C)Ps.

**Actions**
- The Surgery & Anaesthetics Directorate clinicians are reminded of the non-Formulary status of esomeprazole and are asked to ensure that patients have tried suitable therapeutic doses of both Formulary PPIs (lansoprazole and omeprazole) prior to esomeprazole.
- The Mental Health Drugs & Therapeutics Committee addressed the matter of initiation of escitalopram by issue of the consensus statement shown on page 4.
- Work is ongoing in the acute directorates to ensure that clinicians and other relevant prescribers are aware of the non-Formulary (and non-SMC) status of buprenorphine patches. Use of medicines not accepted for use by the SMC should be exceptional, in line with the NHSGGC Non-Formulary Prescribing Policy.
- GPs are reminded of the importance of returning forms when asked to prescribe non-Formulary items. Work will continue to ensure requests are appropriate.

**Number of NF requests by medicine**

In total, 37 different medicines were reported via the process; the most common are shown in Table 2.

In the first quarter of 2009-10, the most commonly requested drug was pregabalin. Due to a change in Formulary status, this has not been examined in detail but will be reviewed for future reports.

**Esomeprazole**

This was the most widely requested medicine to March 2009, accounting for approximately 23% of all completed forms. More than half of requests came from the Surgery & Anaesthetics Directorate. Of those, the majority originated in Stobhill or the Royal Alexandra Hospitals.

In 67% of cases, the forms indicated that the patient had failed to respond to at least one other PPI prior to the recommendation for esomeprazole. All cases initiated by GPs noted the patient had failed to tolerate, or respond to, at least one other PPI.

**Medicines**

<table>
<thead>
<tr>
<th>Medicine</th>
<th>2008-09 number of prescriptions</th>
<th>Cost (£ per prescription)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esomeprazole</td>
<td>48,663</td>
<td>£1.8m (37.12)</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>656,190</td>
<td>£3.3m (50.01)</td>
</tr>
</tbody>
</table>

**Escitalopram**

11 of the 13 requests came from prescribers within the Mental Health Partnership. The Formulary alternative, citalopram, had only been tried previously in two cases.

**Medicines**

<table>
<thead>
<tr>
<th>Medicine</th>
<th>2008-09 number of prescriptions</th>
<th>Cost (£ per prescription)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escitalopram</td>
<td>23,366</td>
<td>£56k (24.77)</td>
</tr>
<tr>
<td>Citalopram</td>
<td>290,578</td>
<td>£579k (9.11)</td>
</tr>
</tbody>
</table>

In response to this information, the Mental Health Drugs & Therapeutics Committee issued the following statement:

contd on page 4
Towards safer use of anticoagulants

Learning points

• The dose and flow rate must be prescribed on the infusion chart. Refer to Therapeutics: A Handbook for Prescribers for information on dose and rate, including monitoring and adjustment of doses.
• Consider how different strengths of heparin injection are stored to minimise errors caused by selecting the wrong product. Most wards will not require to stock higher concentrations of heparin. Only the ready diluted preparations such as heparin 1000units/ml (10 or 20ml vials) should be used for heparin infusions.
• Ensure regular checks of syringe drivers. This is especially important with high risk, high consequence drugs such as heparin.

New oral anticoagulants

Two new oral anticoagulant agents, rivaroxaban and dabigatran, are licensed for the prevention of venous thromboembolism (VTE) in adults undergoing elective hip or knee replacement surgery. Detailed information is available in the recent PostScript Extra at www.ggcformulary.scot.nhs.uk

• Rivaroxaban has been added to the Formulary, restricted to use in VTE prophylaxis in orthopaedic surgery. The NHSSGC protocol which will outline its exact place in therapy is awaited.
• Initial studies have shown rivaroxaban to be superior to SC enoxaparin for the prevention of VTE following elective hip or knee replacement surgery.
• Initial studies did not show any statistically significant difference in bleeding risk; however, further studies are required to confirm this.
• There are no studies comparing rivaroxaban with aspirin.
• If prescribed within NHSSGC, the full treatment course of rivaroxaban should be supplied from hospital prior to discharge.

PostScript Extra 16:
Clopidogrel and possible interaction with PPIs

In PostScript 52 we published a consensus statement from the NHSSGC Heart Disease Managed Clinical Network following the EU Committee for Medicinal Products statement on the possible interaction between clopidogrel and proton pump inhibitors (PPIs). This statement highlighted studies that suggest clopidogrel may be less effective in patients receiving PPIs. This could result in patients being at increased risk of thrombotic events, including acute myocardial infarction.

Clinicians have been reporting difficulty in interpreting this advice and there has been much debate on whether the interaction is more theoretical than a significant clinical issue. Common clinical scenarios are provided in PostScript Extra 16 in a Q&A format as a guide to clinical practice. If prescribers are still unsure how to proceed, specialist advice should be sought from the patient’s cardiologist or gastroenterologist. In general, prescribers should:
• avoid the use of a PPI with clopidogrel if possible,
• consider if comitant therapy is appropriate:
  - is clopidogrel indicated?
  - has aspirin been tried previously?
  - is there a need for a PPI?

Non-Formulary reporting in primary care

“NICE issued an update to their ‘Depression in Adults Guideline’ (No 90) in October 2009. Contained within this is a review of escitalopram. The summary of the findings is as follows:
• Escitalopram is superior to placebo and the 20mg dose is probably more effective than 10mg but at the cost of increased side effects.
• Escitalopram is at least as effective as other antidepressants but is no better tolerated than sertraline.
• Differences in effect that favour escitalopram versus other SSRIs are not thought to be clinically significant.
• There is no evidence of additional benefit versus venlafaxine and duloxetine.
• Cost of escitalopram remains high compared with other antidepressants.

The view of the Mental Health Drugs & Therapeutics Committee is that escitalopram is a high cost antidepressant with no observable clinical benefit over existing Formulary choices of antidepressants. Therefore it should not be used within the existing antidepressant algorithm. Escitalopram remains a non-Formulary option with NHSSGC.”

Buprenorphine patch

3 of the 14 requests were started by GPs. The remainder were requested by the Surgery & Anaesthetics Directorate; mainly via pain clinics. Half of those requests originated in Gartnavel General Hospital. In most cases the patients had failed to tolerate, or respond to, alternative analgesia up to weak opioid level (codeine/tramadol).

It is likely that very little transdermal buprenorphine is initiated for inpatients and so largely bypasses the acute non-Formulary process. There is some inpatient use with variation in prescribing practice between sites. Work is ongoing with the Rehabilitation and Assessment Directorate to provide information on audit and usage patterns for information and action by the management team.