Rivaroxaban is now first choice for DVT and PE

Rivaroxaban is now the first choice option for the treatment of deep vein thrombosis (DVT), pulmonary embolism (PE), and the prevention of recurrent deep vein thrombosis (DVT) and PE in adults in NHS Highland (except Argyll & Bute). The change in guidance means patients will have a simpler treatment regime, and it will reduce the number of patients being initiated and maintained on warfarin.

Patients currently prescribed enoxaparin and/or warfarin for these indications should remain on these agents unless there is a good clinical reason for switching to rivaroxaban.

The new guidance follows the Scottish Medicines Consortium’s acceptance of rivaroxaban for PE and DVT. The Highland Formulary and NHS Highland shared clinical guidelines have been updated, and prescribers are asked to familiarise themselves with the details contained within these documents (available from 1 October, see NHS Highland intranet).

Although the first line treatment has changed, the length of treatment remains the same. Patients requiring more than 12 months’ therapy should be switched from rivaroxaban to warfarin after about three months of rivaroxaban because the SMC guidance recommends rivaroxaban for up to 12 months only. There is guidance in the Highland Formulary regarding switching from rivaroxaban to warfarin. The second line treatment option is enoxaparin followed by warfarin.

Patients with active cancer should be treated with enoxaparin for the entire treatment course because it has been shown to be the most effective agent in these patients.

To allow early initiation of treatment, pre-labelled packs of rivaroxaban 15mg x two tablets are available for holding in emergency departments and primary care emergency centres. These packs can be used while waiting for a confirmed diagnosis.

Patients in Argyll & Bute should be managed as before following local guidelines.

New safety restrictions for metoclopramide

New restrictions have been placed on the use of the antiemetic metoclopramide following a European review of its safety. These restrictions mean that metoclopramide should only be prescribed for short-term use, defined as up to five days of treatment.

The review was conducted by the European Medicines Agency’s Committee on Medicinal Products for Human Use. It confirmed the well-known risks of neurological effects such as short-term extrapyramidal disorders and tardive dyskinesia. However, the review concluded that these risks outweigh the benefits in long-term or high-dose treatment. Therefore, it recommended a restriction to the dose and duration of use to help minimise the risk of potentially serious neurological adverse effects.

The review recommends a maximum dose for adults of 30mg in 24 hours, usually given as 10mg up to three times a day or 0.5mg per kg of bodyweight. The risk of acute neurological effects is higher in children than in adults and therefore use in children is restricted further. This includes metoclopramide being contra-indicated in children aged below one year.

In NHS Highland, palliative care experts have advised that there may be palliative care circumstances where these recommendations may not provide optimum treatment. Specialist advice is available either from the Highland hospice tel 01463 243132 or from the PCAS service 01463 705546 at Raigmore Hospital.

Further details are available in the August edition of the MHRA Drug Safety Update.

Triptorelin licence updated

Triptorelin is still the Highland first choice intramuscular gonadorelin analogue for patients with prostate cancer, and now its licensed indications have been extended. These include: (i) neoadjuvant treatment prior to radiotherapy in patients with high-risk localised or locally advanced prostate cancer and (ii) adjuvant treatment to radical prostatectomy in patients with locally advanced prostate cancer at high risk of disease progression.

Leuprorelin is in the Formulary for when subcutaneous injection is needed.

In this issue of the Pink One

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- Page 3: Medicines abuse, diclofenac, sitagliptin
- Page 4: Dermatonics, Formulary

About the Pink One

The Pink One is published by NHS Highland Pharmacy Services. It is circulated to all GPs, hospital medical staff, pharmacists in primary and secondary care, nurse prescribers, charge nurses and to local service managers and directorate managers for onward dissemination to other nursing staff. Views expressed are those of one or more of the editors/contributors.

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Treatment failures with nitrofurantoin

In August, the MHRA highlighted the risk of treatment failure if nitrofurantoin is used in patients with renal impairment. Nitrofurantoin is already contraindicated in patients with a creatinine clearance below 60ml/min because of this risk.

NHS Highland’s antimicrobial management team has raised concerns about this advice with the MHRA. It believes that the evidence behind the decision is limited and is also concerned that precluding use of nitrofurantoin among a significant number of older people will result in increased use of cefalexin (a beta-lactam) as an alternative. This would drive the selection of multi-drug resistant extended spectrum beta-lactamase (ESBL) producing organisms that commonly cause urinary tract infections.

However, until further clarity is obtained, the MHRA advice should be followed. When managing urinary tract infections in older patients, prescribers are reminded to consider the diagnosis carefully. The prevalence of asymptomatic bacteriuria in elderly patients (up to 57% of women in care homes) renders urine dip stick and subsequent urine culture results generally unhelpful. In this population, there is no place for routine urine screening or dip stick testing. Antibiotic treatment should be based on the presence of symptoms. Similar recommendations apply to patients with an indwelling catheter because the majority will have bacteria in the urine. NHS Highland has a shared clinical guideline algorithm for diagnosis of UTI.

In addition, simple non-drug measures such as adequate hydration and good toilet hygiene can reduce the incidence of infection.

For patients who require an antibiotic, recent culture and sensitivity information should be considered. Advice can be sought from Raigmore’s Microbiology Department.

Reminder of pulmonary effects with nitrofurantoin

A patient in NHS Highland recently experienced an acute pulmonary reaction to nitrofurantoin, and therefore prescribers are reminded of this potential adverse reaction.

Clinical presentation of acute pulmonary reactions include: fever, chills, cough, chest pain, dyspnoea, pulmonary infiltration with consolidation or pleural effusion on chest x-ray, and eosinophilia. These reactions usually occur within the first week of treatment. Chronic pulmonary reactions can also occur, although rarely. Prescribers are reminded to monitor respiratory conditions, especially in older patients receiving long-term nitrofurantoin therapy. If pulmonary reactions are suspected, nitrofurantoin should be discontinued immediately. Symptoms are usually reversible with cessation of therapy.

Epistatus: prescribe midazolam by brand name

Epistatus is the midazolam oral solution 10mg/ml preparation of choice in NHS Highland. This is for clinical and safety reasons and to ensure patients and their carers receive the product they have been trained to administer and are familiar with. Therefore, Epistatus should be prescribed by brand name.

In July, Alliance Healthcare became the sole distributor of Epistatus to pharmacies and dispensing GP practices in the UK. Information about ordering Epistatus is available from Alliance Healthcare.

Epistatus preparations were added to the electronic version of the June 2013 Vision Highland Formulary and should be automatically included to GP practice formularies once this update is installed. For practices that do not use the Highland Formulary updates in Vision, Epistatus can be manually added to the practice formulary as follows:

- Select Utilities
- Select Drug Dictionary
- Select Formulary
- Select Maintain
- In the Maintain Formulary screen, tick Special (right hand side), enter epistatus as the drug name and click Find
- Double Click on each Epistatus preparation or click Change on each Epistatus preparation – “i” will appear next to each preparation
- Click Close.
Prescribed medicines: be aware of abuse and misuse

All those involved in prescribing and dispensing medicines should be aware that many prescribed medicines are commonly misused, abused or sold. This is a significant problem locally, and recent work by the NHS Highland substance misuse team has identified current trends in the misuse of prescribed medicines.

Lisa Ross, clinical harm reduction nurse specialist, says: “The list of drugs in circulation seems to be expanding constantly. Different areas of Highland have different drug trends. Trends are often based on what other drugs are available and the quality of street heroin at the time.”

The table (right) lists the current reported street value of some prescribed medicines across Highland.

It is not just patients who may be misusing or abusing medicines: friends and relatives may be abusing or stealing medicines from patients.

If a medicine that has significant potential to misuse or abuse is being prescribed, those prescribing and dispensing should:

- Review the on-going clinical need for the medicine, perhaps more frequently than other medicines.
- Be alert to patients requesting higher doses and/or additional treatments claiming that the current dose or treatment “is not working”.
- Be alert for patients requesting lower strengths but greater quantities of a medicine. This is because a tablet or capsule can have the same street value regardless of its strength.
- Be alert for early requests, particularly if being prescribed on a repeat basis. Minimum prescription interval functions on GP computer systems can be used to restrict issues of prescriptions.

Community pharmacists should be alert to emergency requests for such medicines and consider whether need is genuine. For these medicines it would be prudent only to supply a minimal quantity until the patient can contact his or her GP practice.

<table>
<thead>
<tr>
<th>Prescription medicine</th>
<th>Reported street value</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diazepam 10mg tablets</td>
<td>£1 per tablet</td>
<td>20 tablets sell for £15</td>
</tr>
<tr>
<td>Diazepam 5mg tablets</td>
<td>50p per tablet</td>
<td>2x5mg preferred to 1x10mg</td>
</tr>
<tr>
<td>Dihydrocodeine 30mg tablets</td>
<td>50p per tablet</td>
<td>Depends on local trends</td>
</tr>
<tr>
<td>Tramadol 50mg capsules</td>
<td>Up to £1 per capsule</td>
<td>Usually bought and taken in bulk, whole prescription sells for £10</td>
</tr>
<tr>
<td>Gabapentin tablets/capsules</td>
<td>50p per tablet/capsule</td>
<td>Usually bought and taken in bulk, whole prescription sells for £10</td>
</tr>
<tr>
<td>Pregabalin capsules</td>
<td>50p per tablet</td>
<td></td>
</tr>
<tr>
<td>Quetiapine 200mg tablets</td>
<td>£1-£3 per capsule</td>
<td></td>
</tr>
<tr>
<td>Suboxone 8mg tablets</td>
<td>£8 per tablet</td>
<td></td>
</tr>
<tr>
<td>Methadone mixture</td>
<td>£10 per 40ml</td>
<td></td>
</tr>
<tr>
<td>Nitrazepam 5mg tablets</td>
<td>£1.50-£2 per tablet</td>
<td></td>
</tr>
</tbody>
</table>

Current Highland street values of some prescribed medicines

Diclofenac now contraindicated in CV disease

Further concerns about the cardiovascular safety of diclofenac have resulted in it becoming contraindicated in patients with:

- Ischaemic heart disease
- Peripheral arterial disease
- Cerebrovascular disease
- Congestive heart failure (NYHA classification II-IV).

Extra care should be taken before using diclofenac in patients with significant cardiovascular risk factors such as hypertension, hyperlipidaemia, diabetes or smoking.

Affected patients should be switched to an alternative treatment at their next routine appointment. Naproxen and low-dose ibuprofen have a lower thrombotic risk than other NSAIDs. However, all NSAIDs should only be used at the lowest effective dose and for the shortest duration of time to control symptoms.

The new advice was issued by the MHRA following a Europe-wide review of NSAIDs. It found that the cardiovascular risk of diclofenac is similar to that of the selective COX-2 inhibitors.

Accurate renal function needed for sitagliptin

Renal function must be calculated accurately in obese patients with type 2 diabetes in order to ensure safe prescribing of sitagliptin.

Renal function is routinely reported as eGFR, however this is inaccurate at extremes of body weight. Since patients with type 2 diabetes are commonly overweight, eGFR may therefore be an over-estimate of actual renal function.

The dose of sitagliptin should be reduced in patients with reduced renal function. If renal function is over-estimated, it would result in too high a dose of sitagliptin being prescribed.

Therefore, in obese patients with type 2 diabetes who have known CKD and a reduced or borderline normal eGFR (<60), consider either:

- Calculating renal function using the Cockcroft and Gault equation (BNF p18) using ideal body weight; or
- Adjusting eGFR using actual body mass index.

Linagliptin may be a better option.

<table>
<thead>
<tr>
<th>News in brief</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Codeine safety concerns</strong></td>
</tr>
<tr>
<td>New restrictions have been placed on the use of codeine in children following safety concerns. They include restricting codeine to children older than 12 years and only when paracetamol and ibuprofen have been ineffective. Codeine is contraindicated in all children who undergo procedures for obstructive sleep apnoea, and is not recommended when breathing might be compromised. The maximum daily dose is 240mg (in divided doses) and limited to three days.</td>
</tr>
<tr>
<td><strong>Pripsen discontinued</strong></td>
</tr>
<tr>
<td>Prispen (piperazine 4g and senna sachets) has been discontinued. Adults and children over six months can be treated with mebendazole; however this is unlicensed for children under two years. Pregnant women or children under two years of age should, in the first instance, attempt to eradicate threadworm infestation by rigorous hygiene. Specialist advice should be sought before treating pregnant women and children under six months.</td>
</tr>
</tbody>
</table>
Dermatonics useful for diabetic foot care

Patients with diabetes are advised to moisturise their feet daily using emollients such as Diprobase or Epaderm. Despite this, some patients develop anhydrotic or rough dry skin on the plantar aspect of the foot which can become cracked and infected. This is prevalent in a large proportion of ulcerations.

To treat this cracked, dry skin, Dermatonics Once Heel Balm has been added to the Highland Formulary. It contains 25% urea and is applied once a day to hard skin. Urea has keratolytic properties which help to remove the callus.

In many cases, Dermatonics will be used as a one-off treatment for around three months.

However, some people may require continual treatment. The use of this product should form part of an individually tailored plan in conjunction with podiatric care.

Complications of the diabetic foot are common, complex and costly. All patients with diabetes must have their feet evaluated at least yearly for the presence of predisposing factors for ulceration and amputation. Where abnormalities are present, more frequent evaluation is recommended.

Through systematic examination and risk assessment, patient education, and timely referral to podiatry services, the unnecessarily high prevalence of lower-extremity morbidity in this population may be reduced.

Reduce risks for IV iron

Strengthened measures to minimise the risk of serious reactions to intravenous iron products have been introduced. The reactions include life-threatening and fatal anaphylactic and anaphylactoid reactions. As a result IV iron products should:

- Not be used in patients with known hypersensitivity.
- Only be used in high risk patients if benefits clearly outweigh risks.
- Not be used during pregnancy unless clearly necessary and only in the second or third trimester.
- Be administered with caution for every dose, with close monitoring for at least 30 minutes afterwards.
- Only be administered where resuscitation facilities are available.

Highland Formulary news and updates: September 2013

Changes agreed in September 2013 to the Highland Formulary are shown below. The Highland Formulary document has been updated with these changes and is available on NHS Highland Intranet at http://intranet.nhsh.scot.nhs.uk/Clinical/Formulary/Pages/Default.aspx and website at www.nhshighland.scot.nhs.uk. Highland Formulary decisions on recent SMC advice are also available on NHS Highland Intranet and website.

"Highland Formulary 5th edition"

The Highland Formulary 5th edition is available on the NHS Highland Intranet and website and as a free App for iOS. This e-version is updated bimonthly and should be referred to for the most up to date Formulary information.

A paper copy of the 5th edition is being distributed in September to those on the Formulary distribution list.

Ferric carboxymaltose (Ferinject)

Ferric carboxymaltose intravenous infusion has been accepted onto the Formulary for the treatment of iron deficiency in non-haemodialysis dependent renal patients. It allows for a larger dose to be given in one visit and therefore minimises patient, travel and nursing time.

Colobreathe

Colobreathe (colistimethate sodium) is an easy to use and convenient breath actuated device. It will be used in patients with cystic fibrosis colonised with Pseudomonas aeruginosa whose respiratory symptoms remain poorly controlled (or whose lung function continues to decline) despite current best treatment.

Latanoprost single dose eye drops

Single dose latanoprost eye drops are now available. They are a useful preservative free formulation for patients intolerant of the preservative in the multi-dose eye drop preparation.

List of changes to the Highland Formulary agreed in September 2013

The full cumulative list of changes to the Highland Formulary 5th edition is provided in the e-Pink One document, available on NHS Highland Intranet and website.

Addition of medicines

Chapter 2
Argatroban solution for infusion 100mg/mL (Exembol)

Chapter 4 Central nervous system
Trifluoperazine syrup 1mg/5mL
Clozapine suspension 50mg/1mL
Tramadol m/r tablets 50mg
Clonazepam oral solution 500 micrograms/5mL

Chapter 5 Infections
Nitrofurantoin capsules 50mg
Rifaximin tablets 550mg
Colimethamate sodium inhalation powder 1,662,500 units (125mg)

Chapter 6 Endocrine
Vasopressin, synthetic (Argpressin) injection 20 units/1mL

Chapter 9 Nutrition and blood
Ferric carboxymaltose (Ferinject) solution for injection/infusion 100mg iron/2mL, 500mg/10mL
Glucose intravenous infusion 20% Albumin solution 5%

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Medicines Information service
NHS Highland Medicines Information service: email nhshighland.medicineinformation@nhs.net, tel 01463 704288, address: Pharmacy, Raigmore Hospital, Inverness IV2 3UJ.
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Glucose intravenous infusion 20%
Albumin solution 5%

Chapter 11 Eye
Latanoprost preservative-free single-dose eye drops 50 micrograms/mL

Deletions
Chapter 4 Central nervous system
Memantine tablets 5mg/15mg

Chapter 5 Infections
Piperazine 2 dose sachet pack (piperazine 4 grams, sennosides 15·3mg/sachet)

Chapter 9 Nutrition and blood
Albumin solution 4%
Volulyte infusion
Voluven infusion

Chapter 13 Skin
Zinc and castor oil ointment