LOTHIAN PRESCRIBING BULLETIN

Supporting prescribing excellence - informing colleagues in primary and secondary care

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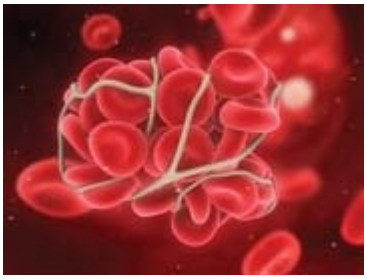
In this issue …

Oral anticoagulants – what's new?

Dabigatran and rivaroxaban are new oral anticoagulants for the prevention of stroke in non-valvular atrial fibrillation (AF). Dabigatran directly inhibits thrombin and rivaroxaban directly inhibits factor Xa.

The pivotal studies for dabigatran (RE-LY) and rivaroxaban (ROCKET-AF) had similar primary end points of a composite of prevention of stroke (ischaemic or haemorrhagic) and systemic embolism. The **RE-LY trial** showed dabigatran 110mg twice daily was non-inferior to warfarin, whilst the higher dose of 150mg twice daily was shown to be statistically superior. There was no difference in all cause mortality. Gastrointestinal bleeding was reported statistically significantly more often with dabigatran 150mg twice daily than warfarin, but caused significantly less life threatening or intracranial bleeding.

The **ROCKET-AF trial** showed that rivaroxaban was non-inferior to warfarin. The pre-specified test for superiority in the safety population was demonstrated for rivaroxaban versus warfarin. There was no difference in major and non-major clinically significant bleeding between rivaroxaban and warfarin. Intracranial haemorrhage and fatal bleeding was significantly less with rivaroxaban, but gastrointestinal bleeding was significantly more common.



There is no head to head data or guidance on how to choose between dabigatran or rivaroxaban. The trials had similar primary end points, the methodologies were different.

The Scottish Medicines Consortium has issued advice saying that they are cost effective and suitable for use in NHS Scotland (September 2011 for dabigatran[1] and February 2012 for rivaroxaban[2]). Furthermore Healthcare Improvement Scotland (HIS) has issued a consensus statement on how dabigatran may be implemented in the NHS.

In Lothian a submission was made to the Formulary Committee (FC) to include dabigatran in the Lothian Joint Formulary. FC did not approve the submission and dabigatran is classified as 'not preferred, as suitable alternatives exist'. The main concerns of the committee were safety and the management of bleeding. A submission has not yet been made for rivaroxaban.

Key Messages

- ***Dabigatran is not included in the formulary. A submission for rivaroxaban has not yet been made.***
- ***Patients will be aware of the significant media interest surrounding these new drugs and may ask for them. Prescribers should ensure that patients are aware of the facts surrounding efficacy and safety.***
- ***Despite their relatively short half-lives (faster 'onset' and 'offset' of action compared to warfarin) there is a significant concern at the lack of antidote should a patient present with life-threatening haemorrhage or require emergency surgery.***
- ***The lack of need to monitor anticoagulation has advantages for the patient, but may cause problems in assessing adherence or identifying drug interactions, with potentially serious consequences.***
- ***Both require dose adjustment in renal impairment and dabigatran requires regular monitoring of renal function.***
- ***These drugs are significantly more expensive than warfarin even when taking into account the costs associated with anticoagulation service.***

References

1. The Scottish Medicines Consortium. SMC No 672/11. Dabigatran etexilate (Pradaxa®). Accessed 20/04/12. www.scottishmedicines.org.uk/files/advice/dabigatran_Pradaxa_FINAL_August_2011_Amended_05.09.11_for_website.pdf.
2. The Scottish Medicines Consortium. SMC No 756/12. Rivaroxaban (Xarelto®) atrial. Accessed 20/04/12. http://www.scottishmedicines.org.uk/files/advice/rivaroxaban_Xarelto_for_AF_FINAL_Jan_2012_for_website.pdf.

Unlicensed 'Specials' – not so special?

Special-order products ('specials') are unlicensed medicines that have not been assessed by the regulatory authority for safety, quality and efficacy in the same way as licensed preparations. 'Specials' can be obtained from a range of sources (hospital or commercial supplier with a manufacturer's 'specials' licence) and are not all manufactured in the same way. This means that the quality, bioavailability, consistency and cost of specials can vary even where the same product is prescribed.[1] 'Specials' may have a short shelf-life compared with licensed preparations and may need to be stored in a fridge.[2]

As with any medicine, the prescribing of unlicensed 'specials' is the responsibility of the prescriber signing and issuing the prescription. However there are several additional considerations. The prescriber must be satisfied that an alternative licensed medicine would not meet the patient's clinical needs (e.g. a different drug in the same class) and that there is a sufficient evidence base and/or experience of using the medicine to demonstrate its safety and efficacy.

Prescribers must also take responsibility for regularly reviewing the ongoing need for a 'special' to ascertain that it remains clinically appropriate for the patient.

Patients (or carers) should be made aware when prescribed medicines that are unlicensed, and given accurate and clear information that meets their needs, including information on side effects. As with licensed medicines, any unwanted effects should be reported through the yellow card scheme (www.mhra.gov.uk/yellowcard).[1,3] Pharmacists also have professional responsibilities and they share accountability with the prescriber for supplying a 'special' to a patient.[4]

Pharmacists should be satisfied that the prescriber is aware that the medicine they have requested is only available on an unlicensed basis and where appropriate, provide advice on alternative licensed products.[4]

It is good practice for pharmacists to ensure that chosen suppliers are offering the best all round service, taking into account quality, promptness of supply and value for money.[4]

The policy in NHS Lothian is that where possible, licensed products will be used.

However it is recognised that the use of an unlicensed medicine is sometimes necessary in order to provide optimum treatment for a patient. Any liability associated with the use of approved unlicensed medicines will be accepted by the employing authority provided that best practice has been followed, as outlined in the Policy for the use of unlicensed (and off-label) medicines in NHS Lothian.[3]

'Specials' can be expensive and prescribers are often unaware of their potential high cost. NHS Lothian's primary care annual spend on 'specials' is estimated to be in excess of £2.2 million, the latest available quarter (Q2 2011/12) being £602,837. Prescribers are advised to discuss the costs associated with prescribing and supply of 'specials' with pharmacy colleagues, including where they are concerned about variations in price.[4]

NHS Lothian Specials - Examples of Procurement Price Variation Quarter 2, Financial Year 2011/12

Product	Quantity	Example of lower price paid	Example of higher price paid	Q2 Total Expenditure*
omeprazole suspension 10 mg in 5 mL	300 mL	£46.62	£540.04	£77,538
melatonin 3 mg tablets	60	£4.99	£343.19	£72,146
megestrol acetate 40 mg tablets	100	£304.50	£700.97	£26,766
clobazam suspension 5 mg in 5 mL	300 mL	£36.60	£334.75	£22,784
diltiazem 2% cream	30 g	£49.99	£262.75	£16,218
quetiapine suspension 100 mg in 5 mL	100 mL	£71.35	£353.32	£11,439

*Total spend on all strengths of preparations

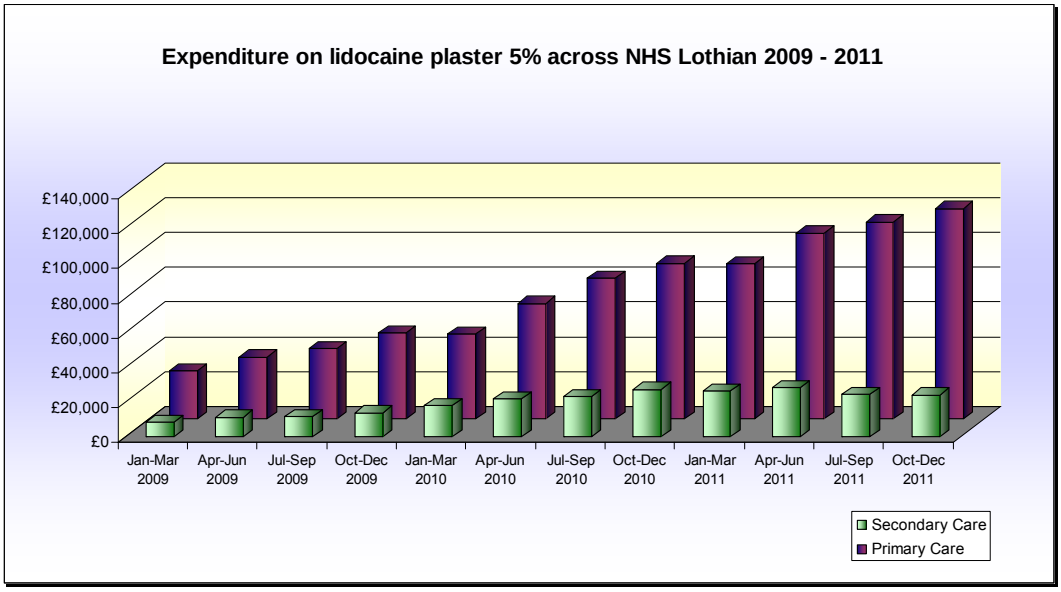
References

1. Prescribing Specials, Five guiding principles for prescribers, National Prescribing Centre. National Institute for Health & Clinical Excellence. 2011. Accessed 20/04/11. www.npc.co.uk/improving_safety/prescribing_specials/resources/5_guiding_priciples_V2.pdf
2. UKMi. Medicines Q&A 294.2: Therapeutic options for patients unable to take solid oral dosage forms. January 2011. Accessed 20/04/11 www.nelm.nhs.uk/en/NeLM-Area/Evidence/Medicines-Q--A/Therapeutic-options-for-patients-unable-to-take-solid-oral-dosage-forms/
3. Policy for the use of unlicensed (and off-label) medicines in NHS Lothian. Version 2, June 2008. Accessed 20/04/11. http://intranet.lothian.scot.nhs.uk/NHSLothian/NHS%20Lothian/BoardCommittees/AreaDrugTherapeutics/Documents/Policy%20for%20the%20use%20of%20unlicensed%20(and%20off-label)%20medicines%20in%20NHS%20Lothian%20-%20Version%202.pdf
4. Royal Pharmaceutical Society. Good Practice Guidance on the procurement and supply of pharmaceutical specials. Pharmacy Professional. Update June 2011. Accessed 20/04/11. www.rpharms.com/support-pdfs/ppjune2010-specials-june2011updatefinal.pdf [RPS members only.]

Avoid a sticky situation – use lidocaine plaster properly

As detailed in the Lothian Joint Formulary (LJF), ***lidocaine 5% medicated plaster (Versatis®)*** is licensed to be used topically for the treatment of post-herpetic neuralgia in those patients who are intolerant of first-line systemic therapies or where these therapies have been ineffective. LJF first and second line treatments for neuropathic pain are amitriptyline and gabapentin respectively. Lidocaine plasters have also been approved in Lothian for use in palliative care (off-label). In paediatrics, they are recommended for second line treatment for persistent neuropathic pain in children who have not responded to gabapentin and amitriptyline.

Expenditure on lidocaine plasters in Lothian is shown in the following table:



The steady increase in expenditure has raised concerns about prescribing patterns. Known non-formulary uses include pain associated with fractures, back pain and other types of neuropathic pain. Anecdotally the patches have also been used for other indications, however use in other pain types has not been studied extensively. As the plaster works by local contact, it is not suitable for treatment of diffuse pain.

It is often possible to discontinue the plaster without the pain recurring as the local effect on nerve endings persists after the plaster is removed. If the pain resolves completely, try a plaster free period after seven days of plaster use:

- **Remove the lidocaine plaster(s) for 24 hours and assess the patient.**
- **If the pain returns or worsens, restart the lidocaine plaster.**
- **If the patient remains pain free or with stable pain discontinue the lidocaine plaster.**

Appropriate review of efficacy is vital to ensure that prescribing is stopped if the product is not effective. Most patients will respond within two weeks. If there has been no benefit in two to four weeks or if any response is attributed solely to the skin protective properties of the plaster, discontinue treatment as potential risks may outweigh benefits.

If treatment is continued, reassess with a further plaster free trial on a monthly basis to determine whether treatment can be discontinued, the number of plasters covering the affected area can be reduced or if the plaster-free interval can be extended.

A monitoring sheet is available in the Lothian Palliative Care Guidelines (www.palliativecareguidelines.scot.nhs.uk/documents/LidocainePlaster_Nov09.pdf). This can be used when a patient is started on a lidocaine plaster and updated each time the patient is reassessed.

Key messages:

- **Lidocaine Plaster 5% (Versatis®) is approved in Lothian for post-herpetic neuralgia (in patients intolerant of LJF 1st and 2nd choice) and in palliative care.**
- **If no response to treatment in two to four weeks of initiation, discontinue.**

Thanks to Anne Young, Primary Care Pharmacist, for contributing this article.

Bits and pieces – but still important, the sequel

Detailed below are some important reminders and some 'snippets' you might have missed over the last few months.

University Hospitals Division (UHD) Antithrombotic guidelines version 3.2
The antithrombotic guidelines for UHD have been updated. Any paper copies of the previous versions should be destroyed.
The new guidance can be found on NHS Lothian intranet:
Healthcare>A-Z>Haematology>Policy Documents

Tapentadol modified release tablets
Tapentadol is a new novel analgesic with two modes of action; it is a μ-opioid receptor agonist and a noradrenaline reuptake inhibitor. It is a schedule 2 controlled drug. Tapentadol has been shown in trials to be as effective as oxycodone in chronic non-cancer pain.
Following a positive opinion from the Scottish Medicines Consortium (SMC) for modified release tapentadol, the chronic pain team made an application to Formulary Committee (FC) for inclusion in the formulary to replace modified release oxycodone for chronic pain as a second choice opioid. This was approved by the FC.
It should be noted that this is for chronic non-cancer pain and for the modified release formulation only. The immediate release formulation is not recommended for use in NHS Scotland by the SMC, therefore is not approved for use in NHS Lothian.

Antibiotic leaflets
The editorial team thought that readers might like to know about an information leaflet produced by the Royal College of General Practitioners (RCGP). This leaflet supports the article in last month's LPB on antibiotic prescribing. The leaflet is called 'When should I worry?'.
The Health Promotion Service Resource Centre has ordered a supply of these leaflets and all Lothian general practices will be sent a sample copy once received. Further supplies will be available through the Resource Centre. (For more information visit *NHS Lothian intranet>NHS Lothian>Training & Development>A-Z>Health Promotion Resource Centre*)
In the meantime it is possible to purchase these leaflets from the RCGP.

Introduction of new medicines
The Scottish Government issued a CMO letter in February relating to the introduction of new medicines into use in NHS Scotland (SGHD/CMO(2012)1).
The letter sets outs guidance on the timeframes for the introduction of new medicines into practice, how to identify when a new medicine has therapeutic advancement and considerations for Individual Patient Treatment Request (IPTR) arrangements.
Some processes in Lothian require to be amended, as the arrangements are finalised full details will appear on the LJF website News section.
The CMO letter can be viewed via this link.

Hydromol®
Hydromol® ointment is joint second choice (ointment based) emollient in the LJF Section 13.2.1
Hydromol® cream is not a formulary product. There is a large difference in price if the cream is prescribed instead of the ointment. 500g cream costs £11.09, 500g ointment costs £4.74.
The LJF section should be referred to for full details of the formulary choices.

Supplement: Recent SMC and Lothian Formulary Committee Recommendations

The supplement can be accessed via the LJF website www.ljf.scot.nhs.uk in 'Prescribing Bulletins'.

Supplement: Lothian Prescribing Indicators 2012/13 in general practice

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