LOTHIAN PRESCRIBING BULLETIN

Supporting prescribing excellence - informing colleagues in primary and secondary care

Issue No. 9

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In this issue ...

Improving the life of the patient or the patent?

Prescribers will now be only too familiar with the introduction of subtle new versions of medicines shortly before the patent is due to expire. On occasion companies will withdraw medicines before the patent protection lapses, allowing the new substitute to gain a foothold in the market before generic companies can start selling the older drug.

When a new form of an existing medicine is marketed by the existing patent holder, prescribers should consider the following questions:

- Is it more effective than the existing preparation?
- Is it more convenient for patients to take?
- Are patent expiry, generic competition and price reduction of the existing product imminent?

THE LIFE EXPECTANCY OF A PATENT

Current European Union patents for chemical entities are usually valid for 20 years. Since drug development generally takes about 10 years, companies have a limited time to recoup development costs and profit from the drug before patent expiry and availability of generics drives prices down[1]. For many branded medicines, sales are at their greatest by the time the patent expires.

"NEW AND IMPROVED"

The basic patent is rarely the only protection involved. Additional patents for other chemical forms may also extend the effective patent life of a product.

New Formulations

New formulations such as modified release or soluble preparations, that supersede older products, can extend the life of a branded medicine. Current examples are orodispersible formulations of mirtazapine (Zispin SolTabs®) and lansoprazole (Zoton FasTab®). The mirtazapine patent expires this year, and lansoprazole patent will expire in 2005. In the case of mirtazapine, the conventional 30mg tablets are being phased out and a new range of strengths is being introduced. Prescribing the tablets generically allows either formulation to be dispensed. It is not necessary to make any changes to repeat prescribing records in response to this marketing, unless the patient requires one of the new doses (15mg or 45mg) or has a clinical need for an orodispersible preparation.

Enantiomers

Most older drugs exist as a racemic mixture of two forms, each the mirror image of the other (enantiomer). Enantiomers of the same chemical entity can differ in their pharmacological properties, providing new opportunities in drug development. The new compounds are often marketed as having increased efficacy, more predictable pharmacokinetics or reduced toxicity. These claims may not always be backed up with evidence[2,3].

Examples of drugs originally licensed as racemates that are now marketed as single enantiomers include esomeprazole (Nexium®) and escitalopram (Cipralex®)[2]. Note that neither drug is in the Lothian Joint Formulary (LJF).

Key messages:

- **When a new form of an existing medicine is marketed, ask yourself if it meets a clinical need or is it related to patent expiry?**
- **The price for the new form may be cheaper now but consider what will happen when the patent expires and generics are available.**
- **Check the LJF - www.ljf.scot.nhs.uk for formulations recommended within Lothian.**

References

1. Brown P. How Medicines are developed and licensed. Prescriber 2002;13 (23)
2. Prolonging market exclusivity of medicines - implications for the NHS. WeMeReC Bulletin 2003,10(2)
3. Mansfield P, Henry D, Tonkin A. Single enantiomer drugs: elegant science, disappointing effect. Clin. Pharmacokinet. 2004,43(5):287-90

Contact the editorial team at ljf@lhb.scot.nhs.uk

"Economy class syndrome" - what advice do we give?

The possible association of venous thromboembolism (VTE) with air flights and long distance travel remains uncertain. There has been a great deal of interest in this condition recently due to high profile media coverage. Deep vein thrombosis (DVT) itself is relatively common with an incidence of 1 per 1000, so it is inevitable that some patients will present with a DVT after an air flight.

There have been many studies undertaken to look at whether there is an association of VTE with air flights. O'Keefe and Baglin have drawn several conclusions from the evidence[1].

- There does appear to be an association between long distance travel (greater then 6 hours) and VTE in patients with additional risk factors.
- Fatal pulmonary embolism is very rare.
- Criteria for high-risk patients are not well defined.

High-risk patients[1, 2]

Previous VTE
Recent MI or stroke
Body mass index > 40kg/m^2
Hormone therapy
Metastatic cancer
Pregnancy
Major surgery in previous 2 weeks
Thrombophilias

The aetiology of VTE in travellers appears to be multifactorial and prolonged immobilisation appears to be the most likely trigger of thrombosis. There is no evidence that the increased room available to business or first class passengers alters any possible risk of DVT.

While the actual risk is undetermined, general practitioners, physicians and pharmacists are being asked to advise people. Advice should be simple and not put the patients at any further risk.

Simple Advice

- Avoid dehydration
- Restrict alcohol, coffee and sedative drug intake
- Exercise the calf muscles in the sitting position if walking is restricted

In addition, there is some evidence that below-knee compression stockings reduce the incidence of asymptomatic DVT, in high-risk patients.

Drug Therapy

Beneficial effects of drug therapy must be balanced against possible side effects. The risk of bleeding with single dose aspirin or low molecular weight heparin (LMWH) is not defined but should be considered. It is essential to discuss risks and benefits with the patient.

Aspirin (150mg, 12 hours before travel)

- No significant evidence of benefit[1].

LMWH (enoxaparin 20mg, 2 to 4 hours before travel)

- Role in travellers remains controversial, but in one study it did appear to reduce the incidence of thrombosis[1].
- Risk of heparin induced thrombocytopenia is low after a single dose of LMWH.
- Low dose LMWH should be reserved for individuals with multiple risk factors and travelling more than 6 hours[2].

Key messages:

- **All travellers should receive simple advice (defined above).**
- **Evidence suggests that below knee compression stockings may be beneficial for high-risk patients when travelling more than 6 hours.**
- **Evidence of benefit of drug therapy is limited.**

References

1. O'Keefe DJ and Baglin TP. Travellers thrombosis and economy class syndrome: incidence, aetiology and prevention. Clin Lab Haem 2003;25:277-281.
2. SIGN 62 Guideline. http://www.sign.ac.uk/guidelines/fulltext/62/index.html

Be alert - BAN to rINN

Both European and UK legislation require the change of drug names from British Approved Names (BANs) to Recommended International Non-proprietary Names (rINNs) by 30 June 2004, where these differ. The aim is to ensure that drugs imported will all have the same active substances name. This is especially important in an environment where movement of health care professionals between countries is common.

It is recognised errors may arise during the transition period until there is familiarisation with the new names (see Stop Press).

To ensure consistency, rINNs should always be used when dispensing, with any discrepancy clearly explained to the patient.

The main areas of risk include:

- inaccurate prescribing
- inaccurate dispensing
- administration
- patient misunderstanding
- potential confusion between drug names

Stop Press ...

Recent reports of confusion between mercaptamine (the new name for cysteamine) and mercaptopurine led to the issue of a drug alert by MHRA[1].

Most of the changes are minor and unlikely to produce confusion, but some new names may look quite different:

BAN (old name)	rINN (new name)
amethocaine	tetracaine
bendrofluazide	bendroflumethiazide
benzhexol	trihexyphenidyl
cysteamine	mercaptamine
dicyclomine	dicycloverine
dothiepin	dosulepin
flurandrenolone	fludroxycortide
hexamine hippurate	methenamine hippurate
hydroxycarbamide	hydroxyurea
methimazole	thiamazole

BAN (old name)	rINN (new name)
methotrimeprazine	levomepromazine
mustine	chlormethine
nicoumalone	acenocomarol
pramoxine	pramocaine
procaine penicillin	procaine benzylpenicillin
quinalbarbitone	secobarbital
sodium ironedetate	sodium feredetate
thymoxamine	moxisylyte
thyroxine sodium	levothyroxine sodium
trimeprazine	alimemazine

It is important to record and report any medication errors resulting from the switch to allow common problem areas during this transition to be identified and addressed.

The National Patient Safety Agency has produced a guidance leaflet for health care professionals. See www.npsa.nhs.uk. Further useful information including a full list of changes and a Q&A briefing may be found at http://medicines.mhra.gov.uk. Laminated sheets produced by MHRA have been distributed through all main professional journals, it is recommended that these are placed in prominent places for easy reference. A full list may also be found in the introduction to the BNF. Useful telephone number: Medicines Information, new RIE (0131 242 2920).

Key messages:

- **rINNs should now always be used to minimise risk.**
- **Now is the time of high risk of error. Double check when in doubt and report any errors.**
- **All changes should be highlighted to patients.**

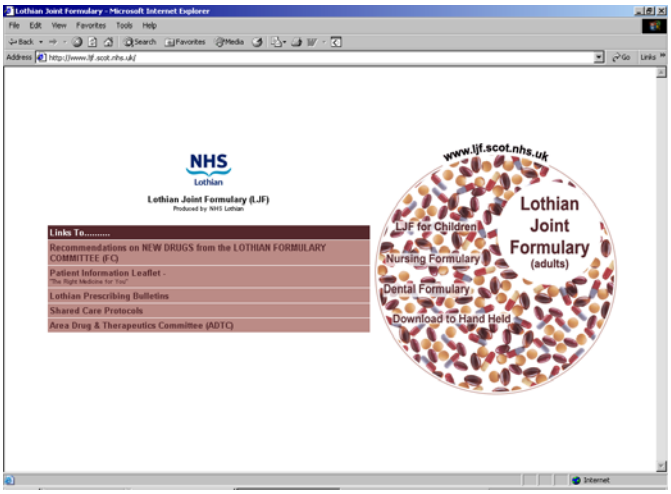
Reference

1. Medicines and Healthcare Products Regulatory Agency, Drug Safety Information. Changes in the names of certain medicines - confusion between mercaptamine and mercaptopurine. 8 June 2004. Available at www.mhra.gov.uk.

LJF News

The website www.ljf.scot.nhs.uk

The web-based version of the LJF is continually updated with amendments that have been approved by the Formulary Committee. The patient information leaflet and Lothian Prescribing Bulletins are available here, as well as links to shared care protocols and the Area Drug and Therapeutics Committee and full Formulary Committee recommendations on new medicines.



The Lothian Joint Formulary - what's new?

The Formulary Committee meets monthly to consider the Scottish Medicines Consortium assessments of new medicines (see the supplement accompanying this newsletter for details) as well as formulary working group reviews of the latest evidence.

Recent amendments include:

- a change from calcipotriol (Dovonex®) to calcitriol (Silkis®)
- the addition of teriparatide (Forsteo®) as a treatment for severe osteoporosis for use by specialists only

The LPB supplement also provides details of new medicines that are not recommended for prescribing. Recently assessed new medicines not recommended for prescribing include ketotifen eyedrops (Zaditen®), valdecoxib (Bextra®), olopatadine eyedrops (Opatanol®), and perindopril with indapamide (Coversyl Plus®).

Patient Information Leaflet

"The Right Medicine for You" is an information leaflet for patients, produced by the LJF Implementation Working Group. If you would like copies please contact the Medicines Management Team (see address below). It is also available on the LJF website.

Fungal nail infections - clip before you treat

Another recent LJF amendment highlights that:

- Treatment for fungal nail infections should not be commenced before mycological confirmation[1].
- In view of the long duration of treatment, possible significant side effects and high costs, cosmetic treatment is not justified.
- Topical agents such as amorolfine should be reserved for cases of early infection confined to the distal edge of the nail.

When treatment is required the LJF recommends:

First choice: terbinafine 250mg daily (6-12 weeks for fingernails; 3-6 months for toenails)
Second choice: itraconazole course of 200mg twice daily for 7 days repeated after 21 days: fingernails, 2 courses; toenails, 3 courses

Reference

1. Guidelines for Treatment of Onychomycosis, 2003 British Association of Dermatologists. Br J Derm 148, 402-10.

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