LOTHIAN PRESCRIBING BULLETIN

Supporting prescribing excellence - informing colleagues in primary and secondary care

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In this issue ...

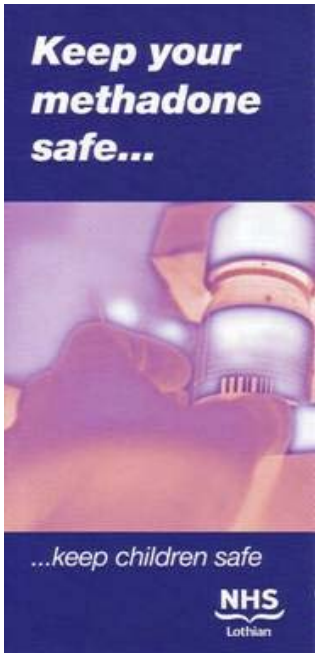
Eptadone® - not recommended in Lothian

A new formulation of methadone hydrochloride, available as Eptadone® 1mg/mL and 5mg/mL oral solution, is not recommended by the Lothian Formulary Committee due to safety concerns. The Lothian Pharmacy Contractors Committee has endorsed this decision. Methadone oral solution 1mg/mL is recommended for use in Lothian.

The view of the Formulary Committee is that this product presents an unacceptably high risk of accidental overdose in the community and is also likely to increase the possibility of potentially fatal dispensing errors. Eptadone® is colourless, does not resemble traditional green methadone 1mg/mL oral solution and it is lemon flavoured, which poses an increased risk to children with potentially fatal consequences.

Although Eptadone® is currently priced below the Drug Tariff price, any cost benefits are significantly outweighed by the potential additional risks.

As a branded generic, this product has not been reviewed by the Scottish Medicines Consortium as it falls outwith its remit.



Methadone Patient Information Leaflet, NHS Lothian, 2006.

Thanks to Elaine Rankine, Specialist Pharmacist in Substance Misuse, NHS Lothian.

'The Bottom Line' No. 1 - early treatment in Bell's palsy

'The Bottom Line' is a new feature in our bulletin which attempts to capture the relevance of some interesting, important articles and clinical trials. The aim is to inform you very briefly and in plain English, about the conclusions and the advice on treatment. "What is the bottom line?" and "How will it change my practice?" are questions you may have asked yourself after reading articles in journals.

Until recently it has not been clear whether treating Bell's palsy with prednisolone or aciclovir aids recovery. A recent double-blind placebo-controlled randomised trial in Scotland has provided the answer.[1]

Treatment	Fully recovered 3 months	Fully recovered 9 months
placebo	65%	85%
prednisolone (25mg twice daily for 10 days)	83%	94%

Aciclovir produced no benefit over placebo, and there was no benefit in adding it to prednisolone.

The Bottom Line:

- Early treatment with prednisolone is effective for Bell's palsy
- Prescribe prednisolone 25mg twice daily for 10 days within 72 hours after onset of symptoms
- Aciclovir is not effective

Reference 1. Sullivan FM *et al*, N Engl J Med 2007;357;*16*:1598-1607.

General practice prescribing indicators 2008/09

The Prescribing Budget Setting Group (PBSG) develops the budget setting formula for general practice prescribing budgets, and also reviews the prescribing indicators (PIs). Two new PIs, for clopidogrel and alendronate, have been introduced this year and targets for other PIs have been revised. The CHPs have agreed to the recommendations in the PBSG Report 2008-09, although the funding of PI incentives is yet to be agreed. For a copy of the full Prescribing Budget Setting Group Report 2008-2009, email: prescribing@nhslothian.scot.nhs.uk.

Prescribing Indicator (PI)	Commentary
Generic prescribing Generic rate ≥ 75% per quarter	Practices must attain this PI to be eligible for incentive payments for the other PIs.
Total antibiotics Items per 100 patients ≤ 70 per annum for all antibiotics	This indicator takes into account the Standing Medical Advisory Committee, Sub-Group on Antimicrobial Resistance report 'The Path of Least Resistance'. Reinforces further guidance on reducing antibiotic prescribing from the Scottish Government.
Co-amoxiclav Items per 100 patients ≤ 5 per annum for co-amoxiclav *(revised target)*	Co-amoxiclav is best reserved for bacterial infections likely or known to be caused by amoxicillin resistant β-lactamase producing strains. Routine use should be discouraged to avoid the development of microbial resistance.
Quinolones Items per 100 patients ≤ 3 per annum for quinolones	These drugs are normally regarded as second line agents. Routine use should be discouraged to avoid the development of microbial resistance.
Hypnotics including temazepam Defined Daily Doses (DDDs) per patient ≤ 1.5 per quarter	In general all hypnotics should be reserved for prescribing in short courses when insomnia is severe, disabling or subjecting the individual to extreme distress.
Modified release (MR) isosorbide mononitrate (ISMN) Plain ISMN prescriptions ≥ 40% of all ISMN prescriptions per quarter *(revised target)*	ISMN is a clinically effective treatment for the management of the symptoms of angina. The benefits of increased patient convenience with once daily MR ISMN should be compared against the increased cost in the individual patient and may be justified in some patients where compliance is an issue.
Angiotensin-II receptor antagonists (ARAs) ARA prescriptions ≤ 25% of all prescriptions for renin-angiotensin system antihypertensives (ARAs + ACEIs) per quarter	The LJF reserves ARAs as an alternative for patients who require angiotensin-converting enzyme (ACE) inhibition but cannot tolerate an ACE inhibitor.
Simvastatin Total number of items of simvastatin ≥ 60% of all statins per quarter	Simvastatin is cost effective compared to other statins. From dosing studies, simvastatin 40mg lowers LDL by 3% more than atorvastatin 10mg and 4% less than atorvastatin 20mg but it has a larger HDL raising effect than atorvastatin 10-80mg.
Oral analgesics Paracetamol 500mg and co-codamol 8/500 and 30/500 tablets prescribed generically as a percentage of all paracetamol and co-codamol tablets and capsules (including effervescent) ≥ 65% per quarter *(revised measure)*	Effervescent or capsule formulations of paracetamol or co-codamol (8/500 & 30/500) are no more effective than the plain tablet versions but are more expensive. There are also concerns that effervescent tablets contain high amounts of sodium.
Wound dressings Wound management products cost per weighted patient ≤ £3.00 per annum	LJF-recommended dressings are cost effective options for the various classes of dressing, prescribing of LJF-recommended wound management products will result in cost efficiencies.
Ulcer healing drugs (UHDs) DDDs per weighted population ≤ 7 per quarter	NICE guidelines state that the lowest possible dose of proton pump inhibitor (PPI) should be used, so the prescribing is to be measured by DDDs with a weighted population to allow for consideration to be given to age, deprivation and mortality ratio.
Esomeprazole Total number of items of esomeprazole ≤ 4% of esomeprazole and LJF recommended PPIs per quarter *(revised target)*	Oral esomeprazole (non-LJF drug) is not recommended for use in NHS Scotland for the prevention of gastric or duodenal ulcers or the healing of gastric ulcers associated with NSAID therapy following assessment by the Scottish Medicines Consortium. No trials have demonstrated a therapeutic advantage of esomeprazole over the other PPIs when the treatments are given at equivalent doses.
Antihistamines Total number of items of desloratadine and levocetirizine ≤ 10% of desloratadine, levocetirizine and LJF recommended antihistamines per annum	There is currently little evidence that third generation antihistamines (desloratadine or levocetirizine - non-LJF drugs) provide any clinical benefit over second generation antihistamines (loratadine or cetirizine).
Escitalopram Total number of items of escitalopram ≤ 10% of all selective serotonin re-uptake inhibitors per annum	There is currently little evidence that escitalopram (non-LJF drug), the *S*-enantiomer of the antidepressant citalopram, is any more effective or has a faster onset of action than citalopram. Escitalopram was launched before the patent for citalopram expired.
Alendronate Total number of items of generic alendronate ≥ 60% of all scripts for oral bisphosphonates prescribed for osteoporosis per quarter *(new PI)*	Alendronate is the LJF-recommended first choice for postmenopausal osteoporosis, first choice treatment and prophylaxis for corticosteroid-induced osteoporosis, and first choice for osteoporosis in men.
Clopidogrel Total number of DDDs of clopidogrel per weighted patient ≤ 0.8 per quarter *(new PI)*	SIGN 93 states that clopidogrel should be combined with long-term aspirin for discrete periods of time (4 weeks or 3 months) depending on the coronary illness. SIGN 97 states that clopidogrel may be used as an antiplatelet in established cardiovascular disease if there is hypersensitivity or intolerance of aspirin. Aspirin is the first choice antiplatelet for secondary prevention in cardiovascular disease and peripheral vascular disease. The LJF provides guidance for the use of clopidogrel or antiplatelets in Lothian.

Diabetes - are you in the right *glita*zone?

There have been many articles regarding increased rates of myocardial infarction and osteoporosis with thiazolidinediones in the general and medical press over the last year. This article aims to summarise the main issues.

Cardiovascular events

A meta-analysis reported a 43% increased risk for myocardial infarction with rosiglitazone[1]. This paper became the subject of much debate and criticism, one being that it used data from study summaries. Another being that none of the included trials were designed to measure cardiovascular outcomes. The United States Food & Drug Administration (FDA) meta-analysis showed a 40% increased risk for ischaemic events with rosiglitazone[2]. Several more meta-analyses, using essentially the same data, have been published, some repeating the original findings. All that is certain is that these are complex analyses where there will always be some doubt.

In theory, a single, large, well-designed study could answer all concerns. One major study (RECORD) is underway and an urgent interim analysis showed no significant differences, but the rate of death and cardiovascular hospital admission was 11% higher with rosiglitazone than with metformin/sulphonylurea[3]. Unfortunately, the trial is underpowered, and it is unlikely that the final results will be conclusive.

These meta-analyses included studies comparing rosiglitazone with placebo, insulin, sulphonylureas, metformin or combinations. If accepted, the worst results show that cardiovascular risk is higher with rosiglitazone than with 'everything else' combined. The questions are "Is adding rosiglitazone better or worse than doing nothing?" and "Is adding rosiglitazone better or worse than starting insulin?" These questions are entirely unanswered.

Enthusiasts claim that the PROactive study showed a 16% reduction in death, MI and stroke with pioglitazone v placebo[4]. Critics say that this is invalid because these were not primary outcomes. A meta-analysis of pioglitazone studies, similar to those for rosiglitazone, reported a statistically significant 18% reduction in the rate of death, MI and stroke[5].

The European Medicines Evaluation Agency (EMEA) recently concluded that the benefits of both pioglitazone and rosiglitazone in the treatment of type 2 diabetes continue to outweigh the risks[6].

They recommended changes to the summary product characteristics (SPC) for rosiglitazone to reflect:

- that in patients with ischaemic heart disease and/or peripheral vascular disease rosiglitazone use is not recommended
- that rosiglitazone is contraindicated in patients with acute coronary syndrome (ACS)

Position statements and warnings generally recommend careful consideration for patients at high cardiovascular risk. Type 2 diabetes carries a risk equivalent to having had a previous MI, and so it is hard to know what this means[7].

Osteoporosis and fractures

Both pioglitazone and rosiglitazone reduce bone mineral density in post-menopausal women[8,9]. In the ADOPT study, the fracture frequencies in women taking rosiglitazone, metformin and glibenclamide were 9.3%, 5.1% and 3.5% respectively; there were no differences in men[10]. MHRA and Takeda UK Ltd (manufacturers of pioglitazone), issued a statement warning of increased fracture risk in women: 2.6%, versus 1.7% with controls in pooled trials[11].

Thanks to Dr Roderick Warren, Dept of Diabetes & Endocrinology, RIE.

Key messages:

- **New patients requiring a thiazolidinedione should be prescribed pioglitazone (LJF first choice) as evidence of cardiovascular risk with rosiglitazone is worrying but less than definitive[12]**
- **If a patient is currently on rosiglitazone, and has a history of ischaemic events or is at significant risk of events or develops an acute coronary syndrome, consider changing them at their next review to pioglitazone or an alternative treatment**
- **Heart failure is a contraindication for rosiglitazone and pioglitazone**
- **The osteoporosis concerns also apply to both drugs, and require a case-by-case decision; they should be avoided in elderly women with high fracture risk, irrespective of cardiovascular risk**

References

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12. Nathan DM. Diabetes Care 2008;*31*:173-5.

The change of LjF–extensive update to HRT section

The Hormone Replacement Therapy LJF sections (6.4.1, 7.2.1) have been updated. Full prescribing information can be found at www.ljf.scot.nhs.uk.

LJF adherence of HRT products is now being measured and this new measure is included in the report recently circulated to practices.

LJF choices

There are only 2 changes to drug choices:

- **Evorel®** (replaces Estraderm MX®)
- **Premique® Low Dose** (replaces tibolone)

Starting HRT

HRT should be prescribed for short term treatment of menopausal symptoms only. There is no evidence that HRT prevents cardiovascular disease; indeed, it may worsen cardiovascular outcome particularly in older women. Although HRT protects against osteoporosis, it is not indicated first line for this as the risk : benefit ratio is unfavourable. The lowest dose of HRT that relieves symptoms should be prescribed.

Oral regimens should be considered as first line as they are cheaper than patches and well tolerated. Considerable individual variation exists in responses to HRT. Women should persevere with a new preparation for 2 to 3 months to allow initial side effects to settle; it may be appropriate to try two or three different preparations.

Breast awareness and attendance at breast/cervical screening should always be encouraged. In most situations, women with premature menopause should be treated with HRT until the age of normal menopause and then be reviewed.

HRT risks and benefits

The table in the LJF (section 6.4.1) detailing the associated risks and benefits of HRT has been extensively updated. It includes useful information on different age groups, cancers, preparations and duration of treatment.

Stopping HRT

The need for ongoing HRT should be reassessed at least annually. Stopping HRT abruptly can cause hot flushes, so treatment should be withdrawn gradually by decreasing dosages over 3 to 6 months. Consider stopping HRT if a woman suffers an acute cardiovascular event, or is at increased risk of thromboembolism due to immobility.

Issues with patches

Estracombi® is still prescribed in Lothian, although it is not in the LJF. It causes more skin irritation than newer matrix patches such as Evorel® Sequi. Local experts advise that it may be appropriate to cut Evorel® Conti patches to provide women with the option of a lower dose, although this is not in the product licence.

Topical oestrogens

Local oestrogens can improve local vaginal and bladder symptoms caused by oestrogen deficiency; systemic therapy is necessary for vasomotor symptoms. Most women with significant vulvo-vaginal problems will require long-term treatment, particularly if sexually active. Women without a uterus can use vaginal oestrogens indefinitely. Women with a uterus can use vaginal oestrogens continuously for 2 years; beyond this, a short course of oral progestogen should be prescribed annually, and investigation of any withdrawal bleeding undertaken.

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eLJF-GPASS v2008 upgrade

The latest version of eLJF-GPASS was recently emailed to all practices. This includes all the latest changes to the LJF and is compatible with the latest drug dictionary, PPD 51. EPASS accredited CPD packs for new users of eLJF-GPASS are available free of charge from MMT or can be downloaded from the LJF website.

Combivent® MDI discontinued

Combivent® metered dose inhaler will not be available after June 2008. It has been discontinued due to ongoing issues relating to the use of CFCs in inhalers. Patients should be reviewed and, if appropriate, switched to two separate inhalers, for salbutamol and ipratropium. Combivent® nebules are still available.

Naproxen OTC for period pain

Naproxen 250mg tablets can now be purchased from pharmacies under the brand name Feminax Ultra® for the treatment of period pain (primary dysmenorrhoea).

Correspondence address:
Medicines Management Team (MMT)
Stevenson House
555 Gorgie Road
Edinburgh
EH11 3LG **Tel: 0131-537-8510**

Email: prescribing@nhslothian.scot.nhs.uk

View the Lothian Joint Formulary at www.ljf.scot.nhs.uk