LOTHIAN PRESCRIBING BULLETIN

Supporting prescribing excellence - informing colleagues in primary and secondary care

Issue No. 14

April / May 2005

In this issue ...

Assessing Cardiovascular Disease Risk: New Treatment Thresholds for Primary Prevention

There has been a significant change in the recommendations for assessing cardiovascular disease (CVD) risk and also in treatment thresholds, and these are now included in the most recent BNF 49, March 2005. The new charts appear at the end of the printed version of the BNF and calculate CVD risk, taking into account the risk of stroke in addition to coronary heart disease (CHD) risk for primary prevention. These charts were recommended in the 2004 British Hypertension Society guidelines[1] and replace the previous CHD risk charts. In addition to the charts the BNF contains a section 'How to use the Cardiovascular Risk Prediction Charts for Primary Prevention' which is essential reading.

Please note:

- CVD risk ≥ 20% is approximately equivalent to CHD risk ≥ 15% (If using 'old' CHD charts multiply by 4 and divide by 3 to get the equivalent CVD risk).
- The new charts no longer differentiate between diabetic patients and non-diabetic patients, because patients with diabetes are now considered to be at high risk. Most people aged over 40 with diabetes should be treated.
- The charts are simplified into 3 age bands.
- Decision to treat with a statin should be discussed on an individual basis. For example, some diabetic patients over 40 and no other risk factors may not require treatment. Some patients may not wish to continuously take a life-long treatment.
- The risk threshold for treatment has changed. In primary prevention, treatment is indicated for people with CVD risk ≥ 20%.
- Lothian lipid guidelines will soon be updated to reflect this decision.

The Lothian Formulary Committee have discussed health economic data for statins in primary prevention relating to the cost effectiveness of this new threshold for treatment and have concluded:

- Cost effectiveness at this new threshold, CVD ≥ 20%, is similar to other therapies that have been accepted for use in the NHS.
- Treatment is cost effective when based on simvastatin 20mg or 40mg doses at current generic prices. The cost effectiveness of treatment with other statins is not known but in some clinical situations may not be cost effective at current prices.
- Expenditure on statins will rise considerably as a result of this new advice.

Key messages:

- **The latest BNF contains new charts for calculating CVD risk for primary prevention.**
- **LJF first choice statin for primary prevention of CVD is simvastatin.**
- **Discuss risks and treatment on an individual basis.**
- **The charts can be a useful aid to discussions with individuals about smoking cessation and lifestyle changes.**

Reference

1. Williams B *et al*. Guidelines for management of hypertension: report of the fourth working party of the British Hypertension Society, 2004 - BHS IV. Journal of Human Hypertension 2004;*18*:139-85. http://www.hyp.ac.uk/bhs/pdfs/BHS_IV_Guidelines.pdf
   (See also Cardiovascular Risk Charts and Calculators. http://www.hyp.ac.uk/bhs/Cardiovascular_Risk_Charts_and_Calculators.htm)

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

Prescribing Unlicensed Medicines - Reducing the Risk

Background

The Lothian Area Drug and Therapeutics Committee (ADTC) published guidelines for the use of unlicensed (and off-label use) of medicines in Lothian in December 2004[1]. Copies are available from Stephanie.Butler@lhb.scot.nhs.uk (ADTC Committee Administrator).

"Unlicensed medicines" are those agents which are yet to receive a UK Marketing Authorisation. "Off-label" medicines are those with a UK Marketing Authorisation which are used for an unlicensed indication or are given via a different route.

Prescribers are often unaware that they are prescribing, or being asked to prescribe, medicines outwith their licensed indication or, if they are aware of the situation, do not know where to get advice as to whether or not it is appropriate to proceed.

If an untoward incident occurs with a licensed medicine due to a product defect or its use in an approved clinical situation (as defined in the marketing authorisation), any liability arising may in part or whole be transferred to the marketing authorisation holders. Should a patient suffer harm as a result of the effects of an unlicensed/off-label medicine then the manufacturer is not liable (unless the medicine was shown to be defective) and a claim against either the prescriber or the pharmacist is less easy to defend. Any legal action would also involve the relevant operating division (if applicable) as a result of employer's vicarious liability.

This policy will provide support for primary and secondary care prescribers and pharmacists in the use of unlicensed and off-label medicines.

Categories of unlicensed/off-label medicines in Lothian

Unlicensed/off-label medicines will be assigned to one of the following categories: green, amber, red or black.

Category	Proposed Prescribing Status Within Lothian	Examples
Green	**Unrestricted General Use** Used widely and in accordance with a respectable, responsible body of professional opinion (e.g. Medicines for Children[2]; SIGN/NICE recommendation; Lothian Joint Formulary (LJF).	Aspirin post MI (off-label)
Amber	**General Use With Restrictions** Use has been evaluated by secondary care Drug and Therapeutics Committee (DTC), the Formulary Committee (FC) and the General Practice Prescribing Committee (GPPC), and its use has been authorised as being 'acceptable'. May require a Shared Care Protocol (SCP). Local use has peer group support. Specific consent not normally required.	Methotrexate once weekly in Crohn's disease (off-label)
Red	**Specialist Use Only** Limited evidence of efficacy available. Rarely used or may have serious potential side effects requiring close supervision. Specific consent may be advisable.	Methotrexate for ectopic pregnancy (off-label) Ritixumab for idiopathic thrombocytopenia (off-label) Dichloracetic acid for Leigh's encephalopathy (unlicensed)
Black	**Not Approved for use**	

Process

- Requests to initiate new treatments for groups of patients using unlicensed/off-label medicines should be submitted to the relevant DTC using the Formulary Application Form 3 (FAF3). This will be available from the LJF website www.ljf.scot.nhs.uk.
- If the DTC deem the submission to be appropriate it will be forwarded to the FC who would provisionally categorise it green, amber, red or black. Medicines categorised as **black** should not be used in Lothian. Medicines classified as **red** would then be placed on the approved medicines list for hospital specialist use only.
- If appropriate (**green** and **amber**), the submission would be forwarded to the GPPC for consideration. GPPC would either endorse the proposed category or discuss the submission further with the FC before agreeing the category. For some medicines categorised as amber, a request for a SCP may be made.
- All medicines categorised green, amber or red would be placed on an approved list of unlicensed medicines. This list will be widely disseminated via the LJF website www.ljf.scot.nhs.uk, the Lothian Prescribing Bulletin and included in the LJF when appropriate.

Continued on next page…

Continued from previous page

The ADTC would endorse this process and deal with appeals from prescribers.

Whilst the decision to prescribe an unlicensed/off-label medicine ultimately rests with the individual prescriber, it is anticipated that, in general, GPs would be expected to prescribe medicines assigned to the green category. Medicines assigned to the amber category may require a shared care approach to prescribing. GPs will not be expected to prescribe medicines assigned to the red category.

Key messages:

- **Prescribers have a responsibility to advise patients that they are being treated with an unlicensed/off-label medicine and provide them with accurate and clear information.**
- **Clinical staff involved in the treatment of a patient with an unlicensed/off-label medicine should be:**
  a) Made aware of its unlicensed/off-label status
  b) Informed of any problems and risks involved and how to deal with them
  c) Given sufficient information to administer and use the product safely and correctly.
- **A consultant asking a GP to prescribe a medicine outwith its licence is responsible for ensuring that the GP is given sufficient information about the product to allow safe and appropriate prescribing.**

References
1. Lothian Area Drug and Therapeutics Committee. Policy for the use of unlicensed (and off-label use) medicines in NHS Lothian. December 2004.
2. Medicines for Children. Royal College of Paediatrics and Child Health. 2nd edition. 2003.

Withdrawal of thioridazine (Melleril®)

Novartis Pharmaceuticals have published a letter informing prescribers about the withdrawal of thioridazine (Melleril®) from the worldwide market, as of June 2005[1], because the benefit/risk profile of thioridazine no longer meets current clinical and regulatory expectations.

Thioridazine (Melleril®) is licensed for use only in adult patients with chronic schizophrenia or acute exacerbations who have failed to respond rapidly to treatment in both cases with appropriate courses of other antipsychotic drugs. A Lothian shared care protocol for thioridazine for the treatment of schizophrenia also currently exists[2].

At present in the UK there are no generic alternatives to Melleril® and the generic companies have no plans to reintroduce thioridazine to the UK market. It is possible that unlicensed products can be sourced from abroad in the near future in order to meet individual patient need. However, this cannot be definitely confirmed at present.

Prescribers are advised to review any patients currently receiving thioridazine. To ensure safe discontinuation of thioridazine and possible switch to alternative medications for the treatment of schizophrenia, we recommend that this is undertaken following discussion with, or referral to, the local specialist mental health team in advance of 30 June 2005.

Key messages:

- **Thioridazine (Melleril®) is being discontinued from June 2005.**
- **Patients receiving thioridazine should be reviewed as soon as possible.**

References
1. http://www.druginfozone.nhs.uk/Record%20Viewing/viewRecord.aspx?id=544145
2. http://www.nhslothian.scot.nhs.uk/primarycarelibrary/2_ClinicalPractice/2_Guidelines/Guidelines.htm#SCPs

Further information
- Thioridazine. Restricted indications and new warnings on cardiotoxicity. LPCT Medicines Bulletin 22 December 2000.

Thanks to Marianne van de l'Isle, Principal Pharmacist - Mental Health, LPCD for contributing to this article.

Launch of the LJF for Children

The Lothian Joint Formulary for Children was launched at the Royal Hospital for Sick Children, Edinburgh in March 2005. Mr Fraser Munro (Chair, Paediatric and Neonatal Drug and Therapeutics Committee), Dr Philip Rutledge (Chair, Formulary Committee) and Ms Catherine Booth (Formulary Pharmacist, Royal Hospital for Sick Children) gave presentations to secondary care clinicians, pharmacists and nurses to explain how the formulary was developed, the advantages of formulary adherence and how it can be used.

Several sections are now complete:

Gastro-intestinal System
Respiratory System
Central Nervous System
Infections
Endocrine System
Musculoskeletal and Joint Diseases
Anaesthesia

Sections on ophthalmology and dermatology are in the process of being developed and will be available on the Internet soon while other sections, including ENT, blood/nutrition/metabolic and cardiology, will also be produced.

The LJF for Children is only available in electronic form and can be viewed at www.ljf.scot.nhs.uk. It has also been integrated within GPASS for use by GPs (eLJF-GPASS). New sections will be added to the website and eLJF-GPASS as they are completed.

Stop Press …

Further update on COX-2 inhibitor, valdecoxib (Bextra®) - voluntary withdrawal

Pfizer have voluntarily withdrawn valdecoxib following reports of serious skin reactions (including Stevens-Johnson Syndrome and toxic epidermal necrolysis), in addition to the cardiovascular risk associated with COX-2 inhibitors. The Committee on Safety of Medicines (CSM) issued a message with full details on 7 April 2005, 'Voluntary suspension of valdecoxib (Bextra®) by Pfizer Ltd', Reference CEM/CMO/2005/5, http://www.mhra.gov.uk/news/bextraddl.pdf.

Your attention is drawn to the advice from CSM about the use of COX-2 inhibitors and the fact that a cautious approach should be taken when prescribing these agents.

Warfarin Guidelines Launch

A launch meeting to support the implementation of the recently circulated ***'NHS Lothian Guidelines for the Management of Patients on Warfarin'*** will be held on **Wednesday 18 May 2005** at 6.15pm to 9.00pm, in the Davidson Lecture Theatre, The Lister, 11 Hill Square, Edinburgh.

If you would like to attend this event, it is essential to reserve a place in advance. Please contact Lizzie McGeechan, Clinical Guidelines Co-ordinator, LPCD or Véronique Athukorala, CGST Team Secretary, LPCD:

☎ 0131 537 8576
Fax 0131 537 8502
email lizzie.mcgeechan@lpct.scot.nhs.uk
veronique.athukorala@lpct.scot.nhs.uk

Correspondence address:
Medicines Management Team
Stevenson House
555 Gorgie Road
Edinburgh
EH11 3LG Tel: 0131-537-8573