NORTHERN IRELAND MEDICINES MANAGEMENT NEWSLETTER

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CHOICE OF NSAID [1-4,10]

All non-steroidal anti-inflammatory drugs (NSAIDs) are associated with gastrointestinal (GI), cardiovascular (CV) and renal side effects. Therefore, if NSAIDs are required, they should be prescribed at the lowest effective dose for the shortest period of time necessary to control symptoms. However, important differences have been highlighted between NSAIDs with respect to their side effect profiles.

Cardiovascular risk
Coxibs (celecoxib and etoricoxib) and diclofenac (at a dose of 150mg/day): are associated with an increased thrombotic risk, about 3 CV events per 1000 users per year.
Naproxen and ibuprofen: the possibility of a small increased risk of thrombotic events cannot be excluded. However this is still considered to be lower than the risk with diclofenac or coxibs.

Is this reflected in practice?
A recent article in PLOS (Public Library Of Science) Medicine highlighted that, despite the known CV risk associated with diclofenac, it is still commonly prescribed in a number of countries. Diclofenac is listed on 74 countries' Essential Medicines Lists (EMLs) while naproxen was listed on only 27. The authors of the article in PLOS Medicine recommend that national EMLs should take account of CV risk when composing EMLs, with preference given to low risk drugs; diclofenac should be removed from EMLs.

What is happening in Northern Ireland?
In Northern Ireland a shift from diclofenac to naproxen as first line NSAID has been seen in recent years: from 2009 to the end of 2012 the number of patients prescribed diclofenac has more than halved. This shift is reflected in other areas of the UK. Applying a 3 in 1000 risk of CV event due to diclofenac to NI statistics:
this reduction in diclofenac use could potentially have prevented approximately 57 CV events.

Action

- The appropriateness of NSAID prescribing should be reviewed widely and on a routine basis.
- If a NSAID is required, selection should take into account individual patient factors, with respect to GI and CV risk.
- Pharmacy and Medicines Management (PMMT) now recommend low dose ibuprofen and naproxen as first line NSAID choice.

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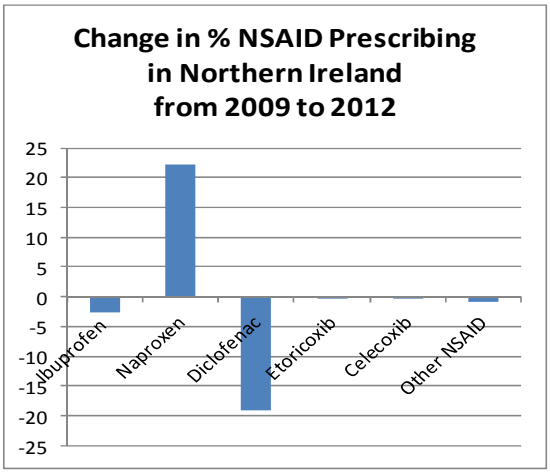
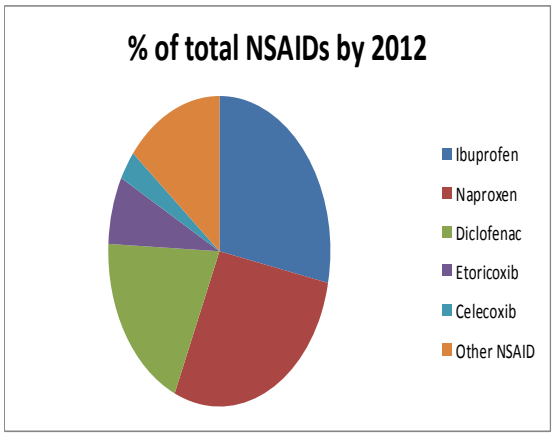




ETORICOXIB — REMINDER OF HYPERTENSION RISK [12-15]

The risks of NSAIDs are well documented. However the risk of hypertension with etoricoxib (Arcoxia®) is less well remembered when initiating and reviewing treatment.

Hypertension is a common side effect with etoricoxib (occuring in >1/100 to <1/10 patients). The Summary of Product Characteristics (SPC) contraindicates etoricoxib in patients with blood pressure persistently >140/90 mmHg. Hypertension should be controlled before treatment with etoricoxib and blood pressure should be monitored within two weeks after initiation of etoricoxib and periodically thereafter.

The MHRA advises that etoricoxib may be associated with more frequent and severe effects on blood pressure than some other COX 2 inhibitors and NSAIDs, particularly at high doses, e.g. 90 and 120mg.

The NICE clinical guideline on Osteoarthritis CG59 recommends against using the 60mg etoricoxib dose as a first-line treatment on the basis of cost-effectiveness.

The EMA assessed the risks of etoricoxib in rheumatoid arthritis and ankylosing spondylitis patients, concluding the use of the 90mg dose ONLY outweighs the risks in these two conditions.

An updated COX 2 review tool (Feb 2013), focusing on the cardiovascular risk and monitoring requirements with high dose etoricoxib (Arcoxia®), has been completed by the Medicines Management Team and is available from your local Medicines Management Adviser on request.

Action

- Clinicians should prescribe etoricoxib in accordance with the above recommendations.
- Patients receiving etoricoxib should be monitored for signs and symptoms of cardiovascular side effects (e.g. fluid retention, high blood pressure, shortness of breath, or chest pain).

NSAIDs + ANTIHYPERTENSIVES — POTENTIAL FOR DRUG-INDUCED KIDNEY INJURY [7]

Acute kidney injury is a major clinical concern, often caused by adverse reactions. Drug-related acute kidney injury is commonly associated with the use of individual classes of drugs, e.g. antiretroviral drugs, aminoglycoside antibiotics, and non-steroidal anti-inflammatory drugs (NSAIDs). However little is known about the effects of drug interactions on this outcome. This is an important consideration in patients with hypertension who require more than one drug for adequate blood pressure control.

A study in the British Medical Journal (BMJ) aimed to retrospectively assess the risk of acute kidney injury in patients prescribed combinations of diuretics, angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) with a NSAID. They reported that use of a double therapy combination (i.e. one antihypertensive plus NSAID) was not associated with an increased rate of acute kidney injury (although the risk was modified by the duration of use of a diuretic-NSAID combination), but that use of a triple therapy combination (i.e. two antihypertensives plus a NSAID) was associated with an overall 31% higher risk of acute kidney injury. This study has some potential limitations, however it highlights the need for pharmacovigilance with these combinations.

Action

- Increased vigilance is warranted when using antihypertensives concurrently with NSAIDs.
- Particular attention should be paid early in the course of treatment.
- More appropriate use and choice among available analgesic drugs could therefore be applied in clinical practice.
- Remember NSAIDs should be used at the lowest dose for the shortest possible time.

YELLOW CARD e-LEARNING [5,6]

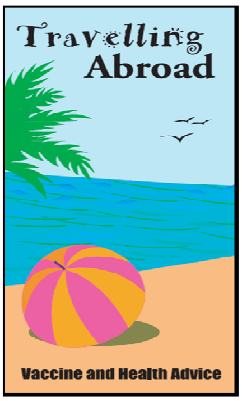
Adverse drug reactions are a major public health concern, and are amongst the leading causes of death in many countries. Effective reporting of drug reactions is an important way for healthcare professionals to contribute to the safer use of medicines. The MHRA have collaborated with BMJ Learning to develop a multimedia learning module, 'Pharmacovigilance—identifying and reporting adverse drug reactions'.

Action

Healthcare professionals who are interested in completing the module can do so at the following link:
http://learning.bmj.com/learning

If a patient experiences a serious or unusual side effect from a medicine, healthcare professionals and members of the public should report this via a Yellow Card at: https://yellowcard.mhra.gov.uk/

TRAVEL INFORMATION[9]



It is coming close to that time of year again when the number of requests for travel advice in primary care increases markedly. Practices are reminded that they should follow the Regional Travel Vaccine Guidance available on the GP Intranet.
Link to the travel information on the GP intranet: http://primarycare.hscni.net/pdf/travel-leaflet-2009.pdf

Travel vaccines
Vaccines NOT available on the NHS for travel purposes:

- Hepatitis B
- Rabies
- Japanese encephalitis
- Meningococcal vaccine
- Tick borne encephalitis
- Yellow fever

When these are required for travel purposes, a private prescription should be issued.

Antimalarial drugs
Malaria prophylaxis is NOT available on an NHS prescription. Anti-malarials should be prescribed on a private prescription. Only chloroquine and proguanil can be purchased from community pharmacies without a prescription.

Medication for travel abroad or travel kits
Items such as anti-diarrhoeals and antibiotics requested "in case" should not be prescribed on an NHS prescription,

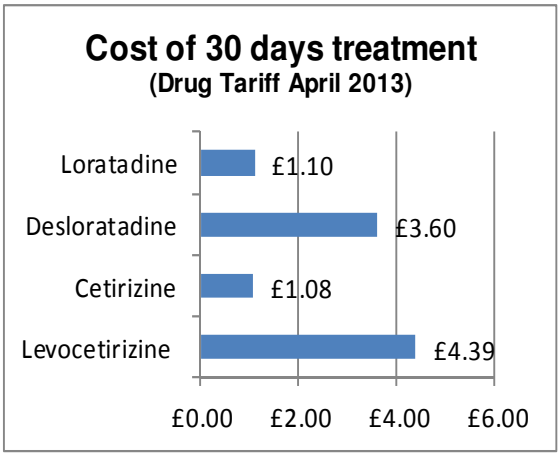
Patients on long term medications…how much should be prescribed?
If a person is going overseas on a temporary basis it is reasonable to give a maximum quantity of 3 months. However, it should be remembered that the prescriber is responsible for any drug monitoring that may be required. If monitoring is required when the patient is away from home, the patient should be advised to consult a GP at their holiday destination for on-going care. If the period of stay is longer than this, patients should be advised to register with a doctor as soon as possible, to allow time for their medicines to be sourced without a gap in treatment.

HAYFEVER — CHOICE OF ANTIHISTAMINE? [9,17-20]

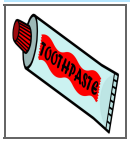
Cetirizine, loratadine or fexofenadine are recommended for treatment of allergic rhinitis (loratadine is preferable in pregnancy). If sedation is an issue, the British Society for Allergy and Clinical Immunology (BSACI) notes that fexofenadine cause the least sedation out of the 'non-sedating' antihistamines.

Levocetirizine and desloratadine are biologically active isomers of cetirizine and loratadine respectively. There is however, little evidence to confirm whether they confer any additional benefit over the more established non-sedating antihistamines.
Cetirizine and loratadine are the most cost effective choices (see chart).

Action
Prescribers are encouraged to prescribe generic cetirizine or generic loratadine as their first-line antihistamine of choice.



PRESCRIBING OF HIGH STRENGTH FLUORIDE TOOTHPASTES IN GENERAL PRACTICE [16]



Oral health is an integral part of general health and therefore poor oral health can have a detrimental effect on quality of life. Dental caries (decay) is one of the main contributors to poor oral health. Fluoride confers significant resistance to dental caries with the topical action of fluoride on enamel and plaque considered more important than the systemic action. Regular tooth-brushing with standard toothpaste is vital in preventing caries. Standard over the counter adult toothpastes contain between 1000 ppm and 1500 ppm of fluoride.

High concentration toothpastes are also available in two strengths, 2800ppm (0.619%) and 5000ppm (1.1%) and can be used to reduce the risk of dental caries in those who are at increased risk of dental caries or are medically compromised. The Department of Health guidance "Delivering Better Oral Health" (April 2009) defines those at risk of dental decay as:

- Undergoing orthodontic care
- Head and neck radiotherapy
- Dry mouth and other predisposing factors, e.g. end of life care
- Special needs
- Obvious current active dental decay

In Northern Ireland the cost of GP only prescribing of high concentration fluoride toothpaste per year is approx. £22,500. The use of these products should only be prescribed following a dental clinical assessment and as part of an overall dental health management plan. **These products should only be prescribed by a General Dental Practitioner (GDP)**.

Action
GPs should identify any patients in their practice who have been prescribed high concentration fluoride toothpastes and advise these patients to attend their General Dental Practitioner for a clinical dental assessment. GPs should not write any further prescriptions for these products.

RED AMBER MEDICINES — REMINDER TO PRACTICES [11]

Prescribing information from the Business Services Organisation (BSO) shows that there are still many "Red Listed Drugs" being prescribed by practices in Northern Ireland despite recommendations that prescribing responsibility should remain with secondary care consultants and supply should be made via hospital pharmacies.

Most frequently prescribed RED list items prescribed in primary care within previous six months (July-December 2012):

Drug	Indications	No of prescriptions prescribed
Thioridazine	Second line treatment of schizophrenia	21
Midodrine	Orthostatic hypotension	21
Chorionic gonadotrophin (Choragon®, Pregnyl®)	Infertility	18
Acitretin (Neotigason®)	Psoriasis	18
Voriconazole (Vfend®)	Anti-fungal	15
Teicoplanin (Targocid®)	Anti-infective	13
Valganciclovir (Valcyte®)	Cytomegalovirus (CMV) in AIDS patients; prevention of CMV during immunosuppressive therapy post organ transplant	13

The Red List is updated on a regular basis, and the current version can be found at the link below:
http://www.ipnsm.hscni.net/library/Red%20Amber%20Lists.html

The Interface Pharmacist Network Specialist Medicines website is easy to use; it contains links to all the current Shared Care Guidelines for each of the clinical specialities:
http://www.ipnsm.hscni.net/library/Shared%20Care%20Guidelines.html

The website also contains contact details for the Interface Pharmacists-Specialist Medicines in each of the five Regional Trusts, along with lots of other useful information.

Action for Prescribers
When presented with a recommendation from secondary care to prescribe medication, and you are unsure of its' red/amber status, please check the website before issuing the prescription.

Action for Community Pharmacists
If you are presented with a prescription for an item which you are not familiar with, please check the website, and confirm the intention of the GP to prescribe, before ordering the medication from the wholesalers.

COST-EFFECTIVE SWITCHES

The Cost-Effective Switch Formulations project aims to achieve savings on named drugs by implementing cost-effective formulations: from specific branded drugs to other branded and generic versions. There are some significant cost differences between the original products and their cost-effective equivalents (see list below. Switches in blue are for new additions for 2013/2014).

From	To
Co-codamol 30/500mg caplets (Solpadol®)	Co-codamol 30/500mg tablets
Co-codamol 30/500mg effervescent tablets	Co-codamol 30/500mg tablets
Co-codamol 8/500mg capsules	Co-codamol 8/500mg tablets
Co-codamol 8/500mg effervescent tablets	Co-codamol 8/500mg tablets
Fluoxetine 60mg (30 days)	Fluoxetine 20mg (x 3 capsules) (30 days)
Levonelle® One Step (OTC)	Levonorgestrel
Migraleve® Yellow tablets	Co-codamol 8/500mg tablets
Nystatin® 100,000 units/mL 30mL suspension	Miconazole oral gel 20mg/g (15g or 80g)
Omeprazole 40mg (7 days)	Omeprazole 20mg (x 2 capsules) (7 days)
Paracetamol 500mg capsules	Paracetamol 500mg tablets
Paracetamol 500mg effervescent tablets	Paracetamol 500mg tablets
Prednisolone E/C 5mg	Prednisolone non-E/C 5mg
Ranitidine Liquid 150mg/10mL 300mL (15 days)	Ranitidine effervescent tablets 150mg or 300mg (adults only) 15 days 150mg bd OR 300mg od
Fluticasone 27.5mcg nasal spray (120 dose) (Avamys®)	Beclomethasone 50mcg/dose nasal spray 200 dose
Fluticasone 50mcg nasal spray (150 dose) (Flixonase®)	Beclomethasone 50mcg/dose nasal spray 200 dose
Momentasone 50mcg nasal spray (140 dose) (Nasonex®)	Beclomethasone 50mcg/dose nasal spray 200 dose
Budesonide 64mcg nasal spray (120 dose)	Beclomethasone 50mcg/dose nasal spray 200 dose
Doxazosin XL 4mg (28)	Doxazosin IR 2mg bd (56)
Gabapentin tablets 800mg 100 capsules	Gabapentin capsules (2 x 400mg) 200 capsules
Paracetamol 500mg/5mL suspension	Paracetamol 500mg soluble tablets or paracetamol 250mg/5mL suspension
Olanzapine oral lyophilisates sugar free (all strengths)	Olanzapine orodispersible tablet SF or non SF
Proctosedyl® ointment	Uniroid HC® ointment
Movicol® sachets (adult -- all flavours)	Laxido® sachets
Xyzal® tablets 5mg	Cetirizine tablets 10mg
Levocetirizine tablets 5mg	Cetirizine tablets 10mg
NeoClarityn® tablets 5mg	Loratadine tablets 10mg
Desloratadine tablets 5mg	Loratadine tablets 10mg
Steripods® saline irrigation fluid 20mL	Irripod® saline irrigation fluid pod 20mL
Saline Steri-Neb® ampoules	Steripoules® sodium chloride ampoules 2.5mg

Action

Practices should consider taking action to implement these switches if they have not done so already, in order to generate significant cost savings for the Health Service. The preferred option should also be considered as first line for new starts if this is the prescriber's drug of choice. Local Medicines Management Advisers are available to offer advice on this if necessary.

RESOURCES OF EVIDENCE-BASED MEDICINE [8]

It is important that the decision to prescribe a medicine (or not) is based on the most up to date evidence available. As information is constantly being updated, on-line sources of information are preferable. There are many sources of information available to healthcare professionals that are free to access. The following are some examples that may be useful:

- BNF (www.bnf.org) and BNF Newsletter (http://www.bnf.org/bnf/org_450066.htm)
- Electronic Medicines Compendium (www.medicines.org.uk)
- NHS Evidence (www.evidence.nhs.uk)
- Eyes on Evidence (www.evidence.nhs.uk/about-us/eyes-on-evidence). A free monthly e-bulletin covers significant new evidence as it emerges with an explanation about what it means for current practice
- NICE (www.nice.org.uk)
- Medicines and Prescribing Centre (www.nice.org.uk/mpc/index.jsp) is a new site following integration of the NPC into NICE.
- NPC legacy site (www.npc.co.uk)
- Clinical Knowledge Summaries (www.cks.nhs.uk)
- MHRA Drug Safety Update (www.mhra.gov.uk/Publications/Safetyguidance/DrugSafetyUpdate/index.htm)
- HSCB Northern Ireland Formulary (www.hscboard.hscni.net/medicinesmanagement/001%20Northern_Ireland_Formulary.html#TopOfPage)
- The Regional Medicines and Poisons Information, based at the Royal Hospital site of the BHSCT, have access to many more information resources and are an excellent reference point (Tel 028 9063 2032; contact details also available inside front cover of the BNF).

Action

Healthcare professionals should ensure that reliable, up to date, resources are referred to on each occasion. It is important that information is checked before recommending new treatments to patients and that patients are reviewed in line with any new evidence.

Addendum: Midazolam Buccal Solutions article, MM Newsletter February 2013

With reference to this article, PMMT would like to clarify that there is the potential for errors to occur because of the *availability* of different strength preparations and not with any specific product.

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This newsletter has been produced for GPs and Pharmacists by the Regional Pharmacy and Medicines Management Team. If you have any queries or require further information on the contents of this newsletter, please contact one of the Medicines Management Pharmacists in your local HSCB office.

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