NORTHERN IRELAND MEDICINES MANAGEMENT NEWSLETTER

Health and Social Care Board

November 2012

Volume 3, issue 5

In this issue:

Did you see…? UPDATED INFORMATION ON SIMVASTATIN INTERACTIONS[1,15]

What is new?

New information on drug interactions with simvastatin has become available. The prescribing information for simvastatin has subsequently been updated to include new contraindications and restricted doses when taken in combination with particular medicines. The MHRA highlighted the issue in their August 2012 Drug Safety Update: http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON180637

Key points to note:

1. Simvastatin is now contraindicated with ciclosporin, danazol and gemfibrozil.
2. The maximum recommended dose for simvastatin in conjunction with amlodipine or diltiazem is now 20 mg/day.

These combinations can lead to increased plasma concentrations of simvastatin, which is associated with an increased risk of myopathy and/or rhabdomyolysis.

Action for prescribers:

Amlodipine and simvastatin are first-line formulary choices in Northern Ireland. Therefore this new guidance will apply to many patients.

Patients already on this combination should be reviewed. Many patients will have been on this combination for some time (presumably without problems) so this may not be urgent for most. There is a low absolute but increased relative risk of myopathy. For most patients the main options will be:

- A dose reduction from simvastatin 40mg to 20mg OR
- Switch simvastatin to atorvastatin*.

NICE advises using a statin with the lowest acquisition cost (providing drug interactions are not an issue). Generic atorvastatin is now available and so may be considered an option.

* Please note that a lower maximum dose of atorvastatin should be considered with diltiazem, with appropriate clinical monitoring. The effect of amlodipine on atorvastatin concentrations is currently not thought to be clinically significant.

Liver function tests should be carried out following a change of statin therapy. For secondary prevention patients, cholesterol levels should also be checked.

"The MHRA has issued a patient information leaflet to explain the recent changes to simvastatin dosing. Please follow the link: http://www.mhra.gov.uk/home/groups/pl-p/documents/websiteresources/con199557.pdf "

OXYCODONE ABUSE

The Drug and Alcohol Monitoring Service (DAMIS) in Northern Ireland has alerted the Public Health Agency (PHA) to a number of reports of young people (17 to 20 year olds) abusing oxycodone in Northern Ireland. The oxycodone in question is in oral form, and appears to have been bought over the internet. The Department of Health in Northern Ireland, PHA and Department of Justice Northern Ireland (DOJNI) are monitoring this. Anyone with additional information on this is asked to contact DAMIS at DAMIS@hscni.net.

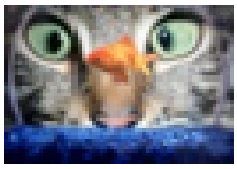
CAUTION WITH TABLET SPLITTING[5,6]

Breaking tablets in half renders most tablets off license and is generally not recommended. However, tablet splitting is common in practice. Reasons for doing so include achieving a different dose from the marketed strengths and cost savings. This can be beneficial but may not be suitable for all patients or all drugs. Tablet splitting does not necessarily result in weight-uniform half-tablets. Studies have shown that there is much variability between tablets. The distribution of active drug in a whole tablet and its potential for crumbling or breaking unevenly are related to drug manufacturing quality assurance standards. Elongated tablets and those with deep score lines, were found to produce more accurate halves. Patient factors can also contribute to accuracy of tablet splitting (visual acuity, strength, dexterity and cognitive ability).

How to minimise errors?

- Avoid drugs with a narrow therapeutic index.
- Avoid enteric-coated and un-scored extended-release formulations.
- Avoid combination tablets in which the amount of one active ingredient changes from one tablet size to the next, but the amount of the other does not.
- Use of tablet-splitting devices may be helpful.
- Patients who are able to split tablets themselves should do so one-at-a-time so that under- or over-dosing could be compensated for by the next dose.

AGE-RELATED MACULAR DEGENERATION (AMD) AND NUTRITIONAL SUPPLEMENTS[8,13]



In the new HSCB Optometric Practice Newsletter, practitioners are asked not to request a patient's GP to prescribe nutritional supplements for Age-related Macular Degeneration (AMD). Such supplements usually contain combinations of vitamins, zinc, omega 3 fish oils, beta-carotene, lutein and zeaxanthin, e.g. Viteyes®, PreserVision® and Ocuvite®.
Nutritional supplements are marketed as exerting a protective effect against the development and/or progression of AMD. However, the current evidence does not support routine use. Evidence for nutritional supplements in AMD is limited to patients with intermediate or advanced AMD in one eye only. Nutritional supplements are classified as food supplements. They therefore lack the product assurance associated with licensed medicines.

Action for prescribers:

Nutritional supplements should not be prescribed for AMD.

Did you see…? TAMIFLU ORAL LIQUID CONCENTRATION[7]

The concentration of Tamiflu® oral suspension has been changed from 12 mg/mL to 6 mg/mL. Patients and carers should be advised that the carton packaging, dosing dispenser and packaging leaflet of the new oral suspension are different from what they may have used in the past. The dispenser has also been changed from milligrams (mgs) to millilitres (mLs). Please see Tamiflu® 6mg/mL Powder for Oral Suspension SPC for further information (www.medicines.org.uk).

ANALGESIC-INDUCED HEADACHES[12]

Clinicians should be aware that people who regularly take medicines, such as aspirin, codeine, paracetamol and triptans could be causing themselves more pain than relief. New guidance issued from NICE makes recommendations on the diagnosis and management of the most common primary headache disorders in young people (aged 12 years and older) and adults (http://guidance.nice.org.uk/CG150). NICE advises GPs and other healthcare professionals to consider the possibility of "medication overuse" in their patients who have been taking medicines for up to half of the days in a month, over three months:

- Triptans, opioids, ergots or combination analgesic medications on 10 days per month or more **OR**
- Paracetamol, aspirin or a NSAID [non-steroidal anti-inflammatory drug, e.g. ibuprofen], either alone or any combination, on 15 days per month or more.

Practices may wish to search for patients taking regular analgesic medicine for headaches and review accordingly.

Management of Medication Overuse Headache:

Explain to people with medication overuse headache that it is treated by withdrawing overused medication.

- Advise people to stop taking all overused acute headache medications for at least 1 month and to stop abruptly rather than gradually.
- Advise people that headache symptoms are likely to get worse in the short term before they improve and that there may be associated withdrawal symptoms, and provide them with close follow-up and support according to their needs.
- Consider prophylactic treatment for the underlying primary headache disorder in addition to withdrawal of overused medication for people with medication overuse headache.
- Do not routinely offer inpatient withdrawal for medication overuse headache.
- Review the diagnosis of medication overuse headache and further management 4–8 weeks after the start of withdrawal of overused medication.

TOPICAL NSAID PRESCRIBING[2-4,14]

What is new?
NICE now recommends topical NSAIDs as first-line pharmacotherapy, alongside paracetamol, for acute flare ups of joint (knee & hand) osteoarthritis. Topical NSAIDs have a favourable safety profile, without the associated systemic adverse side-effects of oral NSAIDs. Full NICE guidance can be found on this link: CG59 Osteoarthritis: full guidance.

Cochrane reviews (2009 and 2012) have found topical ibuprofen, piroxicam, ketoprofen & diclofenac to be of similar efficacy. On the basis of cost, therefore, **PIROXICAM GEL is currently recommended first-line**.

Table TWO: Cost comparisons of topical NSAIDs (as per NI Drug Tariff October 2012 and BNF September 2012)

Product	Pack Size	Price	Prescribing Notes
Ibuprofen gel 5% Ibuprofen gel 5%	100g 50g	£5.52 £2.76	Counselling – photosensitivity Use up to three times daily
Ibuprofen 10% gel	100g	£5.79	Counselling – photosensitivity
Fenbid Forte® (ibuprofen 10%)	100g	£6.50	Counselling – photosensitivity Review after 14 days
Ketoprofen gel 2.5%	100g 50g	£4.02 £2.01	Counselling – photosensitivity Recommended for up to 7 days & Max:15g daily
Oruvail® (ketoprofen 2.5%)	100g	£6.84	Counselling – photosensitivity Recommended for up to 7 days
Powergel ® (ketoprofen 2.5%) Powergel® (ketoprofen 2.5%)	50g 100g	£3.06 £5.89	Counselling – photosensitivity Recommended for up to max 10 days
Piroxicam gel 0.5% Piroxicam gel 0.5%	60g 112g	£2.07 £3.86	Counselling – photosensitivity Use up to 3-4 times daily
Feldene gel® (piroxicam 0.5%) Feldene gel® (piroxicam 0.5%)	60g 112g	£6.00 £9.41	Counselling – photosensitivity Review after 4 weeks
Voltarol emugel® (diclofenac 1%)	100g	£7.00	Counselling – photosensitivity Review after 14 days use, 28 days for OA
Difflam® (benzydamine 3%) cream	100g 35g	£6.84 £2.63	Counselling – photosensitivity
Traxam foam® (felbinac 3.17%) Traxam gel ® (felbinac 3%)	100g 100g	£8.41 £8.03	Counselling – photosensitivity Review after 14 days Max: 25g daily

Note: Topical preparations containing piroxicam are not affected by the CHMP advice on oral piroxicam tablets.

Photosensitivity
Patients should be advised against excessive exposure to sunlight of area treated in order to avoid possibility of photosensitivity. Patients using preparations containing ketoprofen should be advised not to expose area treated to sunbeds or sunlight (even on a bright but cloudy day) during, and for two weeks after stopping treatment; treated areas should be protected with clothing.

Action for prescribers – are you choosing the most cost-effective quantity?
Many clinical systems automatically default to the smallest pack size, which in the case of topical NSAIDs, has inadvertently resulted in expensive OTC brands such as Ibuleve® 30g, Voltarol P® 30g and Oruvail® 30g being prescribed. Default quantities can be set on the Vision Clinical System for the appropriate dispensing pack sizes. This facility is not available on EMIS LV, EMIS PCS and Torex. However, the available pack sizes are listed when the drug name has been selected. Please ensure dispensing pack quantities are specified when prescribing and not "1op" (original pack).

BENZODIAZEPINES AND DEMENTIA[9]

Do benzodiazepines increase dementia?

A recent article in the BMJ reported on a French study that suggested that new use of benzodiazepines increases the risk of dementia by 50%. This study followed just over one thousand elderly adults (average age of 78) for 15 years, none of which were receiving a benzodiazepine at the start of the study. The main difficulty in this study is establishing the exact cause of dementia and the role benzodiazepines play. Many confounding factors were present, including the fact that disturbed sleep can be an initial sign of dementia, so the use of sleeping tablets may be triggered by early dementia and not vice versa. However, the authors conclude that, considering the extent to which benzodiazepines are prescribed and the number of potential adverse effects of this drug class in the general population, indiscriminate widespread use should be cautioned against.

Action for prescribers:
Clinicians should ensure that benzodiazepines are only prescribed when absolutely necessary, in line with national guidance. Only short-term use of benzodiazepines is recommended (up to 4 weeks) due to their side effects and potential for dependency.

HSCB have a range of resources available in relation to the prescribing of benzodiazepines:
http://primarycare.hscni.net/PharmMM_Resources_Clinical%20Resources_Benzos_ZDrugs.htm
This new research which demonstrates an *association* between new benzodiazepine use among elderly adults and the risk of developing dementia, and this information may be of assistance when discussing benzodiazepine use with your older patient population.

Did you see…? CHANGE OF MARKETING AUTHORISATION FOR EPANUTIN® CAPSULES[10,11]

Pfizer have sold the marketing authorisation for Epanutin® capsules to Flynn Pharma. As a result the product has been renamed as 'Phenytoin Sodium Flynn hard capsules'. All other presentations of Epanutin continue to be available as normal (Infatabs®, suspension and solution for injection) from Pfizer Ltd under the Epanutin® brand name. Epanutin® capsules will no longer be available as soon as Pfizer stocks are exhausted.

Phenytoin is a drug with a narrow therapeutic index and, as such, patients should remain on the same brand and formulation of phenytoin. Please note, this product is identical to Epanutin® capsules in all but name:

- Phenytoin sodium Flynn hard capsules are bioequivalent to Epanutin®.
- The site of manufacture remains unchanged (Pfizer).
- The capsules have the same markings and colourings as Epanutin® capsules, including still having the marking 'Epanutin®'.

The change in marketing authorisation has however resulted in a significant cost increase in the product.

Action for prescribers:
Prescribers are advised to specify the Flynn Pharma product for patients currently stabilised on Epanutin capsules. The Flynn product is now listed in the drug dictionary of most clinical systems. It is our understanding that Flynn Pharma is the only supplier to the market place at present. However it is possible that this may change.

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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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