# Derbyshire Medicines Management Newsletter

www.derbyshiremedicinesmanagement.nhs.uk

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The purpose of the Medicines Management newsletter is to deliver succinct, evidence-based advice and information on primary care prescribing issues. Aimed at busy prescribers wanting to know key messages from the many publications in the previous month.



## 1. What's in the news

DTB June 2015,Volume 53 Number 6

Articles relevant to primary care

For full access to the DTB articles login via Open Athens. Those without accounts: https://openathens.nice.org.uk/

Drugs for the doctor's bag: 2- Children

A second part publication by the DTB suggest medicines that a GP might want to have available for use in an emergency or for the acute treatment of children and adolescents. Each section ends with a list of drug recommendations for the doctor's bag trying to avoid repetition for multiple indications. The listed conditions or scenarios are; acute pain, opioid overdose, anaphylaxis, acute respiratory conditions (mild to moderate asthma, severe or life-threatening acute asthma and croup), hypoglycaemia, suspected meningitis/meningococcal septicaemia, nausea and vomiting, gastroenteritis and dehydration and seizures.

Challenges in managing drooling in children

The DTB highlights the difference between anterior (visible) drooling in infancy and that considered neuro-developmentally abnormal when seen in children aged over 4 years of age. Conservative and behavioural management are considered first line options, these include for example 'watchful waiting', and the use of oral motor exercises. The use of the antimuscarinics hyoscine and glycopyrronium is unlicensed and backed only by short term studies with limited evidence.

It is envisaged that primary care clinicians will only consider the prescribing of antimuscarinic following the advice from a MDT. Prescribers are reminded that the use of these drugs is unlicensed.

Protocol for deprescribing

Deprescribing is described as a relevant and valid therapeutic intervention. The application of the principles of deprescribing similar to when initiating drug treatment requires a systematic protocol. Examples of when deprescribing may be appropriate include the use of aggressive anti-hypertensives and hypoglycaemics in older people which may do little to alter the course of the disease while potentially causing hypotension and hypoglycaemia respectively.

The medicines management teams across Derbyshire are undertaking work to help practices to implement deprescribing by providing the necessary tools and guidelines. Please speak to your medicines management pharmacist or technician for more information

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Topical NSAIDs for acute musculoskeletal pain in adults

Derry S, Moore RA, Gaskell H, McIntyre M, Wiffen PJ. Topical NSAIDs for acute musculoskeletal pain in adults. Cochrane Database of Systematic Reviews 2015, Issue 6. Art. No.: CD007402. DOI: 10.1002/14651858.CD007402.pub3

This Cochrane review is an update of 'Topical NSAIDs for acute pain in adults' originally published in Issue 6, 2010.

Authors' conclusions

Topical NSAIDs provided good levels of pain relief in acute conditions such as sprains, strains and overuse injuries, probably similar to that provided by oral NSAIDs. Gel formulations of diclofenac (as Emugel®), ibuprofen, and ketoprofen, and some diclofenac patches, provided the best effects. Adverse events were usually minimal.

Since the last version of this review, the new included studies have provided additional information. In particular, information on topical diclofenac is greatly expanded. The present review supports the previous review in concluding that topical NSAIDs are effective in providing pain relief, and goes further to demonstrate that certain formulations, mainly gel formulations of diclofenac, ibuprofen, and ketoprofen, provide the best results. Large amounts of unpublished data have been identified, and this could influence results in updates of this review.


**This Newsletter has been produced by Slak Dhadli – slakahan.dhadli@southernderbsyhireccg.nhs.uk**

Follow-up of Glycemic Control and Cardiovascular Outcomes in Type 2 Diabetes N Engl J Med 2015; 372:2197-2206June 4, 2015DOI: 10.1056/NEJMoa1414266

The Veterans Affairs Diabetes Trial previously showed that intensive glucose lowering, as compared with standard therapy, did not significantly reduce the rate of major cardiovascular events among 1791 military veterans (median follow-up, 5.6 years). This study reports on the extended follow up of the study participants. The primary outcome was the time to the first major cardiovascular event (heart attack, stroke, new or worsening congestive heart failure, amputation for ischemic gangrene, or cardiovascular-related death). Secondary outcomes were cardiovascular mortality and all-cause mortality

After nearly 10 years of follow-up, patients with type 2 diabetes who had been randomly assigned to intensive glucose control for 5.6 years had 8.6 fewer major cardiovascular events per 1000 person-years than those assigned to standard therapy, but no improvement was seen in the rate of overall survival

JAPC recognises the need for good glycaemic control in patients with Type 2 diabetes, HbA1c targets should be individualised to the patient's circumstances. The Derbyshire glucose control in Type 2 diabetes provides some guidance and consideration in HBA1c target setting.

Hypnotics and cancer risk concerns http://dx.doi.org/10.1016/j.sleep.2015.05.003

The results of a research study using observational data from Finland were widely reported in the media here in the UK. The study published in the journal Sleep Medicine has raised concerns of an association between the **use of hypnotics** and an **increased risk of cancer**, in particular lung cancer. The authors conclude "In this register-based study, sleep-medication use was associated with an increased cancer incidence of the respiratory system. Further studies are needed to examine potential carcinogenic mechanisms associated with hypnotic medications"

Whilst there are limitations to this study clinicians should be aware of this and may use it as a prompt for reviewing historical patients on long term treatment.

**Deleted products 2015 | MIMS online** for June 2015

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| Anafranil SR (clomipramine) | Sonata (zaleplon) |
| BindRen (colestilan) | Rohto Dry Eye Relief (sodium hyaluronate) |
| Zanaflex (tizanidine) | |

## 2. Drug safety update relating to primary care prescribing

(For more information see Drug Safety Update ) Volume 8, Issue 11, June 2015

The website that hosts the Drug Safety Update has now been moved. You can subscribe to alerts by using the following sign up link. Headlines-

- SGLT2 inhibitors (canagliflozin, dapagliflozin, empagliflozin): and the risk of diabetic ketoacidosis (DKA)
  - Serious and life-threatening cases of diabetic ketoacidosis have been reported in patients taking sodium-glucose co-transporter 2 (SGLT2) inhibitors. The MHRA gives advice to prescribers in suspecting DKA and reminds them that this drug class is not licensed for the treatment of type 1 diabetes.
- High-dose ibuprofen (≥2400mg/day): small increase in cardiovascular risk
  - The increase in cardiovascular risk associated with high-dose ibuprofen (≥2400 mg of ibuprofen per day) is similar to that seen with COX-2 inhibitors and diclofenac.
- Intrauterine contraception: uterine perforation—updated information on risk factors
  - Although a rare occurrence the most important risk factors for perforation are insertion during lactation and insertion in the 36 weeks after giving birth

## 3. Local news and GP/pharmacist queries

**GP query**

The IMPROVE-IT study has been published that shows ezetimibe added to a statin now has outcome data in reducing the rate of cardiovascular outcomes. What impact will this have locally in lipid management?

**Answer**

The study enrolled patients between 2005 and 2010 and its reassuring that the trial shows ezetimibe now has clear patient orientated outcome data with reduced cardiovascular outcomes. However, since the trial was undertaken the approach to lipid management has moved on, NICE and local guidance supports the intensification of statins. The IMPROVE-IT study does not show anything unique to ezetimibe over statins and it's the LDL cholesterol effect that is key. A NICE TA review is expected in February 2016 and until then prescribers should continue to follow local guidance.

Memantine untoward incident

A recent admission to DHcFT has raised an issue relating to the prescribing of memantine liquid. A patient with a bottle of memantine liquid 10mg/ml admitted with inaccurate instructions on the bottle label and MAR sheet, incorrectly written as '10ml to be taken……' instead of 1ml for a 10mg dose. An incident cited by the ward staff as not uncommon.

Prescribers are advised to label instructions clearly with the dosage in milligrams and the appropriate volume.

## 4. Quality, Innovation, Productivity and Prevention (QIPP)

Medicines optimisation: discontinuing statin therapy in palliative care
This study provides comparative RCT data for discontinuing or continuing statin therapy in people who were not expected to live longer than 1 year. An American randomised controlled trial found that discontinuing statin therapy in people with advanced, life-limiting illness may not adversely affect clinical outcomes and indeed may improve some important patient orientated outcomes, such as quality of life and reducing overall medication burden. The study supports an individualised approach to stopping or continuing preventative treatment in people with limited life expectancy
The GMC provides useful resource for clinicians and has guidance that provides a framework for good practice when providing treatment and care for patients who are reaching the end of their lives.

Useful resources for patients
GPs are reminded of Patient Information Leaflets produced and updated by DHCS physiotherapists that offer practical advice on exercises that can support their recovery.

MenB and MenACWY vaccination programmes launched in England link
New programmes to protect against meningitis and septicaemia from the Department of Health have been announced; the MenACWY vaccine programme for adolescents from August 2015 and the MenB vaccine for babies aged 2 months from September 2015

Repeat dispensing
Under the 2015-16 pharmacy contracts, local community pharmacies are required to promote repeat dispensing. This may mean practices may have started receiving requests from patients for this to be put in place for them. There are benefits of the repeat dispensing service for patients and prescribers but selecting appropriate patients is key for the success of the scheme. Appropriate is defined as 'patients with long-term, stable conditions who require regular medicines and whose condition is unlikely to change in the short- to medium term'

A Yellow Card smartphone app has been launched (link to MHRA)
The new Yellow Card smartphone app supplements an existing one-stop website and is the only app that allows patients, carers and healthcare professionals to report side effects directly to the Yellow Card Scheme to help MHRA ensure they are acceptably safe for patients

## 5. NICE evidence summaries: New medicines (relating to primary care prescribing )

Ulcerative colitis: budesonide multimatrix (Cortiment)
Summary
Budesonide multimatrix (MMX, Cortiment) is a corticosteroid that is taken orally but exerts its action topically in the colon.
In two 8 week studies, budesonide MMX statistically significantly increased rates of combined clinical and endoscopic remission in adults with mild to moderate ulcerative colitis compared with placebo. However the effect size was small and the clinical relevance of the improvements is unclear. There was no statistically significant difference between budesonide MMX and placebo for clinical improvement and endoscopic improvement at week 8 (secondary end points). It is not known how budesonide MMX compares to other treatments for ulcerative colitis. Adverse event rates were not substantially different for budesonide MMX and placebo
The JAPC is undertaking a review of oral budesonide multimatrix as a treatment option in inducing remission in mild to moderate active ulcerative colitis. Until JAPC agrees on its traffic light status and it's positioning amongst other established treatment options prescribers in primary and secondary should not prescribe this treatment.

Type 2 diabetes: dulaglutide
Summary
For reducing HbA1c levels in people with type 2 diabetes, dulaglutide once weekly, when added to metformin, was statistically superior to exenatide twice daily (both in combination with pioglitazone), statistically superior to sitagliptin and statistically non-inferior to liraglutide 1.8 mg daily. As with the other glucagon-like peptide-1 (GLP-1) receptor agonists there are limited data from randomised controlled trials (RCTs) on the effect of dulaglutide on patient-oriented outcomes, such as rates of macrovascular or microvascular events, or on long-term safety.
Prescribers should note that the annual cost of dulaglutide (both strength) once weekly is £1182.35 compared to the annual costs for other GLP-1 receptor agonists range from £705.75 to £954.84 and no comparative data versus other weekly GLP1 receptor agonists. Dulaglutide is not on our Derbyshire formulary and no proposal has been made for formulary inclusion.

## 6. Useful resources

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| BMJ | www.thebmj.com |
| JAMA: The Journal of the American Medical Association | http://jama.ama-assn.org/ |
| The Lancet | www.thelancet.com |
| The New England Journal of Medicine | http://content.nejm.org/ |
| BMJ, JAMA and NEJM can be accessed in full-text directly through your NHS Athens Account via:<br>National Library for Health:<br>search via My Journals<br>MyAthens:<br>Via National Library for Health Resources or Local Resources.<br>Current Lancet articles are sometimes available with free registration from http://www.thelancet.com/content/register.<br>Print copies of The Lancet are available at DCGH library. | www.library.nhs.uk<br><br>or<br><br>www.athens.ac.uk |
| If you have not already registered for an NHS Athens Account, please register at:<br>NB: It is recommended that you register on a Trust (NHS) PC for speedy confirmation of your username a password. Once registered, your account can be accessed from any computer with online access. | https://register.athensams.net/nhs/nhseng/ |
| UKMI<br><br>Nathnac<br>NHS evidence<br>Electronic medicines compendium<br>Clinical Knowledge Summaries<br>Medicines Prescribing Centre (Formerly NPC)<br>Medicines for children (patient information leaflets<br><br>Drugs in lactation | http://www.ukmi.nhs.uk/<br>https://www.evidence.nhs.uk/search?om=%5B%7B%22srn%22%3A%5B%22%20ukmi%20%22%5D%7D%5D<br>http://www.nathnac.org/<br>http://www.evidence.nhs.uk/<br>http://www.medicines.org.uk/emc/<br>www.cks.nhs.uk.<br>http://www.nice.org.uk/mpc/<br>http://www.medicinesforchildren.org.uk/<br><br>http://www.midlandsmedicines.nhs.uk/content.asp?section=6&subsection=17&pageIdx=1 |
| UK teratology services | http://www.uktis.org/index.html |
| Vaccine update- Vaccination newsletter for health professionals and immunisation practitioners | https://www.gov.uk/government/organisations/public-health-england/series/vaccine-update |