Derbyshire Medicines Management Newsletter

www.derbyshiremedicinesmanagement.nhs.uk

Volume 5 Issue 3 June 2015

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 May 2015,Volume 53 Number 5
Articles relevant to primary care
For full access to the DTB articles login via Open Athens. Those without accounts: https://openathens.nice.org.uk/

Updated guidance on depression in children and young people

In March NICE issued a clinical guideline 'Depression in children and young people: Identification and management in primary, community and secondary care'.
The following are key changes to the previous guideline:

- Offer children and young people with moderate to severe depression a specific psychological therapy (individual CBT, interpersonal therapy, family therapy, or psychodynamic psychotherapy) that runs for at least 3 months.
- Discuss the choice of psychological therapies with children and young people and their family members or carers (as appropriate). Explain that there is no good-quality evidence that one type of psychological therapy is better than the others.
- Consider combined therapy (fluoxetine and psychological therapy) for initial treatment of moderate to severe depression in young people (12–18 years), as an alternative to psychological therapy followed by combined therapy

Primary care clinicians may want to re-familiarise themselves with this NICE guideline when managing the care of children and young people with depression. JAPC endorse the use of fluoxetine in children over 8 years old, after specialist initiation and assessment usually by the CAMHs team.

Impact of HPV vaccination programmes

The DTB reports from authors of a recently published systematic review and meta-analysis funded by the Canadian Institute of Health Research that showed long-term population-level effects of human papillomavirus (HPV) vaccination programmes as promising. The systematic review and meta-analysis included 20 studies and 140 million person-years of follow-up.

In countries with female vaccination coverage of at least 50%, HPV type 16 and 18 infections decreased significantly between the pre-vaccination and post-vaccination periods by 68% (RR 0·32, 95% CI 0·19–0·52) and anogenital warts decreased significantly by 61% (0·39, 0·22–0·71) in girls 13–19 years of age. Significant reductions were also recorded in HPV types 31, 33, and 45 in this age group of girls (RR 0·72, 95% CI 0·54–0·96), which suggests cross-protection. Anogenital warts were also significantly reduced; in boys younger than 20 years of age (0·66 [95% CI 0·47–0·91]) and in women 20–39 years of age (0·68 [95% CI 0·51–0·89]), which suggests herd effects.
In countries with female vaccination coverage lower than 50%, significant reductions in HPV types 16 and 18 infection (RR 0·50, 95% CI 0·34–0·74]) and in anogenital warts (0·86 [95% CI 0·79–0·94]) occurred in girls younger than 20 years of age, with no indication of cross-protection or herd effects

All girls aged 12 to 13 should be offered the HPV (human papillomavirus) vaccination as part of the NHS childhood vaccination programme. Practices are reminded of a PHE/NHSE patient group direction available to improve access and uptake of the HPV vaccine.

Coenzyme Q10 and statin-related myopathy link

Coenzyme Q10 supplementation has been proposed to reduce the adverse muscular effects commonly seen with statin use. Statins causing a reduced endogenous coenzyme Q10 concentration by their mode of action. Coenzyme Q10 is available as a supplement but is not available as a licensed medicinal product in the UK. The DTB notes that NICE do not recommend coenzyme Q10 supplementation to increase adherence to statins and conclude that there is limited evidence that statins cause coenzyme Q10 deficiency and insufficient evidence to identify coenzyme Q10 deficiency as the cause of statin-induced myopathy. They could not recommend the prescribing of coenzyme Q10 on the NHS for statin-related myopathy.

Effects of lithium on renal, thyroid and parathyroid function (Medicines Digest 22nd May 2015 Number 921)

Lithium is a widely used and highly effective treatment for mood disorders, but causes poorly characterised adverse effects in kidney and endocrine systems.

A retrospective analysis aimed to analyse laboratory information system data to determine the incidence of renal, thyroid, and parathyroid dysfunction associated with lithium use was conducted by Oxford University Hospitals National Health Service Trust (Oxfordshire, UK),

1. Adjusting for age, sex, and diabetes, presence of lithium in serum was associated with an increased risk of stage three chronic kidney disease (HR 1.93, 95% CI 1.76–2.12; p<0 ·0001), hypothyroidism (2.31, 2.05–2.60; p<0.0001), and raised total serum calcium concentration (1.43, 1.21–1.69; p<0.0001), but not with hyperthyroidism (1.22, 0.96–1.55; p=0.1010) or raised adjusted calcium concentration (1.08, 0.88–1.34; p=0.4602).
2. Women were at greater risk of development of renal and thyroid disorders than were men, with younger women at higher risk than older women.
3. The adverse effects occurred early in treatment (HR <1 for length of treatment with lithium).
4. Higher than median lithium concentrations were associated with increased risk of all adverse outcomes.

The authors concluded that lithium treatment is associated with a decline in renal function, hypothyroidism, and hypercalcaemia. Women younger than 60 years and people with lithium concentrations higher than median are at greatest risk. Because lithium remains a treatment of choice for bipolar disorder, patients need baseline measures of renal, thyroid, and parathyroid function and regular long-term monitoring

This study adds the importance of clinicians monitoring patients on lithium and following local shared care agreement.

http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(14)61842-0.pdf

Updated advice on use of high-dose ibuprofen

The CMDh (The CMDh is a medicines regulatory body representing the European Union (EU) Member States, Iceland, Liechtenstein and Norway) has endorsed by consensus updated advice on the use of high-dose ibuprofen. This follows a review carried out by EMA's Pharmacovigilance Risk Assessment Committee (PRAC), which confirmed a small increased risk of cardiovascular problems, such as heart attacks and strokes, in patients taking high doses of ibuprofen (at or above 2,400 mg per day). The review clarifies that the risk with high-dose ibuprofen is similar to the risk seen with some other non-steroidal anti-inflammatory drugs (NSAIDs), including COX-2 inhibitors and diclofenac.

The review also looked at data on the interaction between ibuprofen and low-dose aspirin when the latter is taken to reduce the risk of heart attacks and strokes. Laboratory studies have shown that ibuprofen reduces the blood-thinning effects of aspirin. However, it remains uncertain whether long-term use of ibuprofen in clinical practice reduces the benefits of low-dose aspirin in preventing heart attacks and strokes. Occasional use of ibuprofen should not affect the benefits of low-dose aspirin.

The updated advice on the cardiovascular risk of high-dose ibuprofen will be included in the product information of ibuprofen medicines, along with information on the interaction between ibuprofen and aspirin

There is No increase in cardiovascular risk seen with ibuprofen at doses of up to 1,200 mg per day, which is the highest dose generally used for over-the-counter (OTC) preparations taken by mouth in the European Union (EU).

Experimental data suggest long-term use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid (typically 75 mg per day) and until proven conclusively clinicians may continue to offer both treatments if required. No clinically relevant effect is considered to be likely for occasional ibuprofen use

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2015/05/news_detail_002337.jsp&mid=WC0b01ac058004d5c1

Long-term Efficacy of Topical Fluorouracil Cream, 5%, for Treating Actinic Keratosis (Medicines Digest 15th May 2015) Number 920)

932 participants with a mean follow-up duration of 2.6 years aimed to address the question of whether a four week course of topical fluorouracil was effective in reducing the number of actinic keratoses (AKs) over the longer term. Previous studies have shown topical fluorouracil is effective at reducing number of AKs and increases complete AK clearance rates for up to six months compared with placebo.

- The number of AKs on the face and ears per participant was not different between the fluorouracil and control groups at randomization (11.1 vs 10.6, P > 0.10).
- After randomization, the fluorouracil group had fewer AKs compared with the control group at 6 months (3.0 vs 8.1, P <0.001) and for the overall study duration (P < 0.001).
- The fluorouracil group also had higher complete AK clearance rates (38% vs 17% at 6 months) and fewer spot treatments at 6-month intervals, at study visits, and in between study visits during the trial (P <0 .01 for all).
- The fluorouracil group took longer to require the first spot AK treatment (6.2 months) compared with the control group (6.0 months) (hazard ratio, 0.69; 95% CI, 0.60-0.79). The number of hypertrophic AKs was not different between the 2 groups overall (P =0.60), although there were fewer hypertrophic AKs in the fluorouracil group at 6 months (0.23 vs 0.41) (P =0 .05).

The authors conclude that these findings indicate that treating a patient with a single course of fluorouracil would reduce the subsequent number of spot treatments and benefit care of patients with multiple AKs for longer than two years.

Primary care clinicians are reminded to follow our local actinic keratosis guideline.

Pomerantz H, Hogan D, Eilers D, et al. Long-term Efficacy of Topical Fluorouracil Cream, 5%, for Treating Actinic Keratosis: A Randomized Clinical Trial. JAMA Dermatol. Published online May 07, 2015. doi:10.1001/jamadermatol.2015.0502.-http://archderm.jamanetwork.com/article.aspx?articleid=2289130

Antihypertensives and falls in older patients (Medicines Digest 15th May 2015)
Medicines Digest reports of a prospective observational study conducted by Lewis et al concluding no association between antihypertensives and falls in the elderly. 598 community-dwelling patients with hypertension, aged 70 to 97 years, were followed for one year for self-reported falls using monthly calendar postcards and telephone interviews. The authors concluded that given the known benefits of treating hypertension in elderly people, withholding antihypertensive medicines to prevent falls may not be a justifiable medical practice. Although acute administration of any hypotensive can precipitate a fall or syncope, careful up- titration and long-term administration of the lowest effective doses of these medicines do not seem to increase fall incidence.

Reminder for TEMAZEPAM
From 1st June 2015 temazepam is no longer exempt from the prescription writing requirements of Schedule 3 controlled drug. It has the same classification as all Schedule 3 controlled drugs and is subject to prescription writing requirements.

Deleted products 2015 | MIMS online for May 2015

Aqua Maris	Lopresor 50mg tablets
Fortimel Regular	Sterifix
Gastrocote	Xerostom Saliva Substitute Capsules
Gastrocote Liquid	Glucoject no-dol lancets

De-Nol tablets
The manufacturer of tripotassium dicitratobismuthate (De-noltab®) has written to healthcare professionals advising that the product will be discontinued with effect from the end of December 2015. No reason for the decision to discontinue this product is provided in the letter. It is recommended that appropriate alternatives are discussed with any patient who is currently taking this medication as a long term treatment.

2. Drug safety update relating to primary care prescribing

(For more information see Drug Safety Update) Volume 8, Issue 10, May 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

- Sofosbuvir with daclatasvir; sofosbuvir and ledipasvir: risks of severe bradycardia and heart block when taken with amiodarone;

Avoid concomitant use of amiodarone (Cordarone X) with ledipasvir-sofosbuvir (Harvoni), and amiodarone with sofosbuvir (Sovaldi) and daclatasvir (Daklinza), unless other antiarrhythmics cannot be given.
Sofosbuvir (Sovaldi), daclatasvir (Daklinza) and the fixed-dose combination of sofosbuvir and ledipasvir (Harvoni) are direct acting antiviral medicines licensed to treat hepatitis C and are usually supplied from secondary care. Primary care clinicians should try to record these drugs into their clinical systems to future proof against serious drug interactions but be mindful not to issue scripts for them.

- Letters sent to healthcare professionals in April 2015
  - Ketoprofen gel and risk of photosensitivity reactions: reminder of risk minimisation measures – sent on 20 April 2015

FDA warns that SGLT2 inhibitors for diabetes may result in a serious condition of too much acid in the blood (link)
The U.S. Food and Drug Administration (FDA) is warning that the type 2 diabetes medicines canagliflozin, dapagliflozin, and empagliflozin may lead to ketoacidosis. They are continuing to investigate this safety issue and will determine whether changes are needed in the prescribing information for this class of drugs, called sodium-glucose cotransporter-2 (SGLT2) inhibitors.
Patients should pay close attention for any signs of ketoacidosis and seek medical attention immediately if they experience symptoms such as difficulty breathing, nausea, vomiting, abdominal pain, confusion, and unusual fatigue or sleepiness. They are being advised not stop or change their medicines without first talking to their prescriber.
Health care professionals should evaluate for the presence of acidosis, including ketoacidosis, in patients experiencing these signs or symptoms; discontinue SGLT2 inhibitors if acidosis is confirmed; and take appropriate measures to correct the acidosis and monitor sugar levels.

3. Local news and GP/pharmacist queries

GP query
Recently I've had a patient who was given DuoResp 160/4.5 in place of Symbicort by a local pharmacist. The pharmacist said this was now protocol and equivalent to Symbicort 200. Do you know anything about this; if not could you make some enquiries please?

Answer
DuoResp Spiromax is a new breath-actuated dry powder inhaler (DPI) for use in asthma or COPD as a cost-effective 2nd line option (1st line Fostair MDI), where use of a combination inhaler (LABA/ICS) is appropriate.

- DuoResp Spiromax 160/4.5 is equivalent to Symbicort 200/6
- DuoResp Spiromax 320/9 is equivalent to Symbicort 400/12

Both DuoResp strengths are licensed for patients over the age of 18 years and are around £8.00 per inhaler cheaper than Symbicort. The apparent difference in strengths is due to current licensing requirements which state that the dose must be expressed as the 'delivered dose' (the dose that leaves the mouthpiece) rather than the 'metered dose'. For example Symbicort 200/6 will give a delivered dose of 160/4.5, the same as DuoResp.

New patients should be considered for DuoResp Spiromax instead of Symbicort. As for patients already on Symbicort, it is up to practice what they decide to do. Patients may be switched (with appropriate education about how to use their new inhaler) and this will result in significant cost-savings. Community pharmacists may be able to help with this process by signing patients up to the New Medicine Service (NMS) which enables them to spend more time with patients being prescribed new treatments.

It is highly recommended that these combination inhalers should be prescribed by the brand name, rather than generically (e.g. don't prescribe as budesonide/formoterol 200/6) as the devices are operated differently and switching devices without proper explanation may result in patients not using their inhaler correctly. Brand prescribing avoids any potential confusion at the dispensing stage and ensures that the patient will always receive the same brand of inhaler.

This query is similar to the one answered in March and acts as a reminder to clinicians.
http://www.derbyshiremedicinesmanagement.nhs.uk/assets/newsletters/2015/MM_newsletter_volume_4_issue_12.pdf

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

The Senior Prescribers Advisors have agreed across Derbyshire that the following branded generics are accepted onto local guidelines and formularies as cost effective treatment options.

Generic name cost 28 days	Branded generic cost 28 days
Metformin MR as Glucophage in DT 500mg £2.66 750mg £3.20 1000mg £4.26	Sukkarto 500mg £1.73 --------- 1000mg £2.77
Galantamine XL 8mg £51.88 16mg £64.90 24mg £79.80	Luventa XL 8mg £25.42 16mg £31.80 24mg £39.10
Ropinorole MR 2mg £12.54 3mg --- 4mg £25.09 6mg -- 8mg £42.11	Eppinix XL 2mg £5.64 3mg £8.46 4mg £11.29 6mg £15.32 8mg £18.95

Quick tip QIPP
Fusidic acid 1% w/w viscous eye drops 5g is listed in the drug tariff at £13.13. This is significantly more expensive than the formulary first line choice of chloramphenicol 1% eye drops £1.50 for 10ml which has a broad spectrum of activity. Public health England reminds clinicians to treat conjunctivitis if severe, as most are viral and self-limiting. Bacterial conjunctivitis is usually unilateral and also self-limiting (65% resolving by day 5). Where indicated fusidic acid should be reserved for second line use.

Drugs for the doctor's bag: 1–adults DTB — May 2015, Volume 53, Number 5
The DTB maintains that there is still a need for some GPs to carry a range of medicines for use in acute situations when on home visits. They highlight key treatments and suggest choices in some of the more common clinical scenarios that GPs may have to deal with in everyday practice, which may be prior to referral to secondary care. This advice is separate to children's requirements (guidance to follow), the out of hours service and for use within their surgery.

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

Nothing to note

6. Useful resources

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: National Library for Health: search via My Journals MyAthens: Via National Library for Health Resources or Local Resources. Current Lancet articles are sometimes available with free registration from http://www.thelancet.com/content/register. Print copies of The Lancet are available at DCGH library.	www.library.nhs.uk or www.athens.ac.uk
If you have not already registered for an NHS Athens Account, please register at: 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 Nathnac NHS evidence Electronic medicines compendium Clinical Knowledge Summaries Medicines Prescribing Centre (Formerly NPC) Medicines for children (patient information leaflets Drugs in lactation	http://www.ukmi.nhs.uk/ https://www.evidence.nhs.uk/search?om=%5B%7B%22srn%22%3A%5B%22%20ukmi%20%22%5D%7D%5D http://www.nathnac.org/ http://www.evidence.nhs.uk/ http://www.medicines.org.uk/emc/ www.cks.nhs.uk. http://www.nice.org.uk/mpc/ http://www.medicinesforchildren.org.uk/ 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