

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.

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1. Medicines Digest and what's in the news

[DTB | Vol 52 | No 6 | June 2014 - Key primary care headlines of DTB relevant to primary care](#)

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

1. Probiotics and infantile colic

Infantile colic is a relatively common condition and parents will often seek healthcare advice.

Comment: The results of a large double blind placebo controlled randomised trial sample in Australia of breastfed infants and formula fed infants with colic aged less than 3 months, did not support a general recommendation for the use of probiotics to treat colic in infants

Sung V et al. Treating infant colic with the probiotic Lactobacillus reuteri: double blind, placebo controlled randomised trial. BMJ 2014; 348: g2107

2. Implementing drug safety updates Drug Safety Updates are published and circulated each month to UK-based healthcare professionals. Updates often but not always give advice on implementation. Recent examples of advice, such as brand prescribing of anti-epileptics and restrictions on long term prescribing of domperidone and metoclopramide for non-licensed indications have led to problems with implementation.

Regulatory authorities like the MHRA should consult wider with consideration on the practicalities of implementation before publication.

Glycaemic durability with dipeptidyl peptidase-4 inhibitors in type 2 diabetes: a systematic review and meta-analysis of long-term randomised controlled trials

This is the first systematic review and meta-analysis of long-term randomised trials of DPP-4 inhibitors on haemoglobin A1c. Trials were included with at least 76 weeks duration and included the DPP-4 inhibitors sitagliptin, vildagliptin, saxagliptin, linagliptin and alogliptin.

The authors conclude that there is evidence the effect of DPP-4 inhibitors on HbA1c in type 2 diabetes significantly declines during the second year of treatment.

Esposito K, Chiodini P, Maiorino MI, et al. Glycaemic durability with dipeptidyl peptidase-4 inhibitors in type 2 diabetes: a systematic review and meta-analysis of long-term randomised controlled trials. BMJ Open 2014;4:e005442. doi:10.1136/bmjopen-2014-005442

2. Drug Safety Update relating to primary care prescribing

(For more information see [Drug Safety Update : MHRA](#)) Volume 7, Issue 11, June 2014

Combination use of medicines from different classes of renin-angiotensin system blocking agents: risk of hyperkalaemia, hypotension, and impaired renal function—new warnings

Combination use of medicines from different classes of renin-angiotensin system blocking agents is associated with an increased risk of hyperkalaemia, hypotension, and impaired renal function. New warnings have been agreed following an EU-wide review.

Advice for healthcare professionals:

- Combination use of medicines from two classes of RAS blocking agents (ACE-inhibitors, ARBs, or aliskiren) is not recommended.

- In particular, prescribers are advised not to give patients with diabetic nephropathy an ACE-inhibitor with an ARB since they are particularly prone to developing hyperkalaemia.
- The combination of aliskiren with an ACE-inhibitor or ARB is contraindicated in patients with kidney impairment or diabetes.

Patients with heart failure

- Some patients with heart failure may have a medical need for treatment with an ACE-inhibitor and an ARB. Candesartan and valsartan are licensed as add-on therapy to ACE-inhibitors for people with symptomatic heart failure who require such a combination despite optimal therapy.
- The triple combination of an ACE-inhibitor, ARB, and a mineralocorticoid receptor antagonist or other potassium-sparing diuretic is not recommended.

Patients currently taking a combination of RAS blocking agents

- Review the treatment of all patients currently taking a combination of RAS blocking agents at a routine appointment. Carefully consider if combination use is appropriate.
- If combination use is considered absolutely necessary, it must be carried out under specialist supervision and with close monitoring of blood pressure, renal function, and electrolyte levels (particularly potassium). Consider monitoring patients when combination use is started and on a monthly basis thereafter, and also after changing dose and during intercurrent illness.

Ivabradine: emerging clinical trial evidence of increased cardiovascular risk—carefully monitor for bradycardia

The European Medicines Agency is reviewing how the data from the SIGNIFY study impact the balance of benefits and risks of ivabradine. While the review is on-going, prescribers are reminded:

Advice for healthcare professionals:

Posology and monitoring

- The starting dose of ivabradine is 5 mg twice daily. The maintenance dose should not exceed 7.5 mg twice daily.
- Carefully monitor patients for bradycardia or its symptoms (e.g., dizziness, fatigue, and hypotension).
- Down-titrate the dose if resting heart rate decreases persistently below 50 bpm or if the patient experiences symptoms of bradycardia. The dose can be down-titrated to 2.5 mg twice daily if necessary.
- Stop ivabradine treatment if the resting heart rate remains below 50 bpm or symptoms of bradycardia persist.
- Only increase the dose to 7.5 mg twice daily after 3 to 4 weeks of treatment and if the 5 mg dose is well tolerated but insufficient. Carefully monitor the effect of a dose increase on heart rate.

Other considerations

- Avoid concomitant use of ivabradine with heart rate-reducing calcium channel blockers such as verapamil or diltiazem.
- Review the treatment of patients currently using ivabradine where appropriate.

3. Local News and GP queries

GP query

Should patients on sulfasalazine taking enteric coated formulation (or gastro resistant formulation) be changed to plain tablets which are significantly cheaper (£11.93 versus £5.58 for 112 tablets).

Answer

Sulfasalazine plain tabs are licensed to treat ulcerative colitis and Crohn's disease whereas sulfasalazine EC tabs are licensed to treat ulcerative colitis, Crohn's disease and rheumatoid arthritis. So the answer is yes patients can be considered to switch formulations with the exception of rheumatoid arthritis patients. Patients prescribed sulfasalazine EC tablets for rheumatoid arthritis should remain on this formulation. If it is being used for a gastro indication, then a move to plain tablets is reasonable and cost effective.

Evidence of bacterially contaminated over the counter emollients

There is growing evidence and local evidence of bacterially contaminated over the counter emollients being sold from unofficial outlets and over the internet for skin problems.

Consultant dermatologist advice is that if patients suffer recurrent infected eczema, ask them to bring ALL their topicals for review (including any natural or herbal products being used) and check thoroughly. If unexpected discolouration or a film/liquid please swab and inform microbiology of suspicions.

General practical advice for preventing contamination of emollient creams and ointments.

1. Always wash hands before using emollients or ointments
2. Use only licensed medicinal emollients that contain approved preservatives
3. For pump dispensers and tubes:
 - a. Avoid contact with nozzle
 - b. Wipe nozzle clean after use
4. For open pots:
 - a. Before use: decant sufficient emollient into a separate container using a clean spoon
 - b. Do not put hands into pots of emollient (patient or carer)
5. Check product for shelf life and storage

Atrial fibrillation: the management of atrial fibrillation ([NICE](#); accessed July 2014)

In late June, NICE published an update to the management of patients with atrial fibrillation. The recommendation of NICE requires, in some places, a significant change to clinical practice and local guidelines are being developed. In the interim

JAPC has decided to amend the TTR (time in therapeutic range) for warfarin value to NICE recommendations to <65%. If the TTR value is <65% in patients taking warfarin over a 6 month period then this is one criteria used when considering switch to one of the newer oral anticoagulants and been compliant with therapy.

4. QiPP

NP8 prescribing

[The Telegraph](#) published an interesting article with the headline “Pricing scandal sees NHS pay £89 for accessible cod-liver oil capsules”. The article claims the NHS is currently paying up to £89.50 for cod-liver oil capsules with identical versions of which can be bought on the high street for about £3.50. Products like cod liver oil capsules are classed as NP8 products. NP8 products are those products that are not listed in Part VIII of the Drug Tariff and are known as NP8 (NON PART VIII). These drug lines can sometimes be very expensive when prescribed on the NHS and prices can become inflated. They are difficult to monitor by the medicines management team as the prescribing lines in ePact appear under “unspecified codes”. Similar to specials there is nothing unlawful if the endorsement of the cost reflects the cost to the community pharmacy or dispensing practice.

Comment: NP8 lines can be commonly prescribed lines. They can be associated with significant costs if the wrong formulation has been selected or a historical drug line hasn't been updated. For example glyceryl trinitrate [aerosol](#) can cost £75.93 compared to the drug tariff price of glyceryl trinitrate 400micrograms/dose [pump 200D](#) at £3.44. For more information please speak to your practice pharmacist/ technician.

E-Learning modules on adverse drug reactions

With around 1 in 15 hospital admissions attributed to adverse drug reactions, a series of e-learning modules on adverse drug reactions was launched this month. NHS Education for Scotland and the Yellow Card Centre of Scotland has jointly published the six modules. These e-learning modules are written for doctors, nurses and pharmacists—they are especially suited for those in foundation training programmes and those requiring an update in this area for their continuing professional development. The adverse drug reaction e-learning modules can be found at:

<http://www.nes.scot.nhs.uk/education-and-training/by-discipline/pharmacy/about-nes-pharmacy/educational-resources/resources-by-topic/clinical-governance/patient-safety-adverse-drug-reactions.aspx>

'BUMPS'

The UK Teratology Information Service (UKTIS) has launched Bumps. This website provides information leaflets for patients containing facts they need to make informed decisions about using medicines in pregnancy.

'BUMPS' has been set up to enable pregnant women to provide information directly to UKTIS to share with other pregnant women who may need to consider whether or not to take a certain medicine in the future.

The 'BUMPS' website will offer all pregnant women the option to create their own password protected 'my bump's record'. Information entered will be stored anonymously by UKTIS and reviewed periodically to help better understand how the effects that medicines, a woman's lifestyle or the illness for which she was taking the medicine, may affect her baby's development. www.medicinesinpregnancy.org

5. **NICE Evidence summaries: New medicines** relating to primary care prescribing (NICE evidence summaries [link](#)).

New medicines

Long-acting reversible contraception: levonorgestrel 13.5 mg intrauterine delivery system

Summary: In a randomised controlled trial that compared 2 low-dose intrauterine delivery systems containing 13.5 mg and 19.5 mg levonorgestrel (n=2885), the failure rate of the levonorgestrel 13.5 mg intrauterine delivery system (Jaydess: failure rate 0.4% in year 1 and 0.9% over 3 years) was similar to failure rates seen with correct and consistent use of other methods of long-acting reversible contraception. Serious adverse events were reported by 8 women (0.6%) using the levonorgestrel 13.5 mg intrauterine delivery system, including 3 ectopic pregnancies and 2 cases of pelvic inflammatory disease.

The levonorgestrel 19.5 mg intrauterine delivery system used as a comparator in the study is not licensed or available commercially, and there is insufficient evidence comparing the levonorgestrel 13.5 mg intrauterine delivery system with existing contraceptives, including the levonorgestrel 52 mg intrauterine system (Mirena). Two studies are underway comparing this device with a combined oral contraceptive containing drospirenone and ethinylestradiol (Yasmin; NCT01254292) and the progestogen-only subdermal implant (Nexplanon; NCT01397097) respectively.

Comment JAPC reviewed this new LARC formulation and classified it as BROWN 2nd line LARC option after Mirena. The theoretical advantages of a smaller device and lower strength of levonorgestrel are yet to translate or be proven to clinical practice and benefit to patient outcomes.

6. Useful resources

BMJ	www.bmj.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