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 February 2016 Volume 54 issue 2

Evidence for fibrates in secondary prevention of CVD

The DTB reports on a recent Cochrane review that concluded that there is limited evidence to support the use of currently available fibrates for the secondary prevention of cardiovascular disease (CVD).

The findings support recommendations from the National Institute for Health and Care Excellence (NICE) that for secondary prevention of CVD, fibrates should not routinely be offered; NICE guidance also advises that the combination of a fibrate and a statin should not be used for secondary prevention. This is also in line with our local lipid guidance

Adherence to computerised CBT in primary care

A large pragmatic trial has found that computerised cognitive behaviour therapy (cCBT) plus usual GP care does not substantially improve depression outcomes compared with usual GP care alone, raising questions about cCBT's role as a recommended initial treatment for depression.

BMJ 2015;351:h5627

Two new lipid-regulating drugs

Evolocumab and alirocumab are the first 2 propotein convertase subtilisin/klexin type 9 (PCSK9) inhibitors to become available in the UK licensed for primary hypercholesterolaemia and dyslipidaemias. They work by improving the livers ability to recycle LDL receptors, resulting in a greater number of receptors on the cell surface which then enables more LDL-C to be removed from the circulation, resulting in decreased serum LDL-C levels. To date there is limited evidence and no trials with primary outcomes on patient orientated outcomes that show PCSK9 reduce mortality and cardiovascular outcomes.

JAPC reviewed the evidence, cost and patient groups that this treatment could be aimed at and has decided to await NICE recommendations. Following NICE Tas publication, consultation will then begin with lipidologists and cardiologists.

Collagenase Clostridium histolyticum for Dupuytren's contracture

Findings from a Health Technology Assessment report that injections of collagenase C. histolyticum are superior to placebo for the treatment of moderate to severe Dupuytren's contracture. However, surgery remains the most cost-effective treatment based on the available evidence.

Brazzelli M et al. Collagenase clostridium histolyticum for the treatment of Dupuytren's contracture: systematic review and economic evaluation. Health Technol Assess 2015; 19: 1-202

Dipeptidyl peptidase-4 inhibitors and risk of heart failure in type 2 diabetes: systematic review and meta-analysis of randomised and observational studies BMJ 2016;352:i610 http://dx.doi.org/10.1136/bmj.i610

A systematic review and meta-analysis of randomised and observational studies shows that relative effect of DPP-4 inhibitors on the risk of heart failure in patients with type 2 diabetes is uncertain, given the relatively short follow-up and low quality of evidence. They do though suggest that these drugs may increase the risk of hospital admission for heart failure in those patients with existing cardiovascular diseases or multiple risk factors for vascular diseases, compared with no use.

The authors suggest the use of caution when using DPP-4 inhibitors for patients with type 2 diabetes who are at high risk for heart failure.

Bleeding risk: antidepressants & NSAIDs

NICE Eyes on Evidence article reports a large Korean observational study that found antidepressant use with NSAIDs was associated with increased risk of intracranial bleeding within 30 days of first taking the combination. No statistically significant differences were seen between individual antidepressant classes. Although neither SSRIs nor NSAIDs alone have been found to be associated with intracranial bleeding, little is known about whether there is a risk of intracranial bleeding when both medicines are used together.
The EoE concludes evidence supports current BNF and NICE guidance recommending the combination of SSRIs and NSAIDs be prescribed with caution.

Reporting patient safety incidents on the National Reporting and Learning System (NRLS) is clearly important so risks can be identified across NHS England. The learning from these incidents enables action to be taken to improve patient safety e.g. the cascading of patient safety alerts.

Increasing the number of patient safety incidents reported on NRLS, especially from primary care, is a key priority for NHS England. To make the reporting process quicker and easier in General Practice a new GP e-form has recently been launched. A patient safety web page specifically for general practice is also available via the following link http://www.england.nhs.uk/ourwork/patientsafety/general-practice/.

In support of this work, the Specialist Pharmacy Service has developed a step by step guide to help staff in GP practices report medication safety incidents. This guide is aimed at anyone in the GP practice environment who might be reporting medication safety incidents and illustrates the steps using some clinical examples.
http://www.medicinesresources.nhs.uk/en/Communities/NHS/SPS-E-and-SE-England/Meds-use-and-safety/Patient-safety/Promoting-reporting/How-to-Report-Medication-Safety-Incidents-from-a-GP-Practice-on-the-National-Reporting-and-Lea-6356097846/

Deleted products 2016 | MIMS online for February 2016

Acticoat Absorbent	Florinef (fludrocortisone)	Hygroton (chlortalidone)
Savlon Dry (povidone-iodine)	Seractil (dexibuprofen)	Tegaderm Matrix
Voltarol SR (diclofenac		

2. Drug safety update relating to primary care prescribing
(For more information see Drug Safety Update) Volume 9, Issue 7, February 2016

1. Valproate and of risk of abnormal pregnancy outcomes: new communication materials
   To further improve awareness of the risks of valproate in pregnancy new communication materials to support discussion of these risks with women of childbearing potential and girls who take valproate are now available.
   Resources to use (see below for more information):
   - Booklet for Healthcare Professionals
   - Consultation checklist
   - Guide to give to patients
   - Card to give to patients

Later in 2016, the outer packaging for medicines containing valproate will include a warning for women on the risk of adverse pregnancy outcomes

2. Spironolactone and renin-angiotensin system drugs in heart failure: risk of potentially fatal hyperkalaemia.
   Monitoring of blood electrolytes is essential in patients co-prescribed a potassium-sparing diuretic and an angiotensin converting enzyme inhibitor (ACEi) or an angiotensin receptor blocker (ARB) for heart failure.
   Prescribers should refer to the local heart failure guidance which is currently being updated but includes a monitoring section specifically on spironolactone.

Azithromycin

Azithromycin is sometimes recommended as prophylactic treatment by secondary care colleagues in patients with repeated respiratory infections.

Prescribers should note that the correct dose is usually:

500mg to be taken three times a week (e.g. **once daily** on Monday, Wednesday and Friday)

EMA confirms recommendations to minimise ketoacidosis risk with SGLT2 inhibitors for diabetes

Healthcare professionals should be aware of possible atypical cases.

Always consider the possibility of diabetic ketoacidosis in patients taking SGLT2 inhibitors who have non-specific symptoms such as nausea, vomiting, anorexia, abdominal pain, excessive thirst, difficulty breathing, confusion, unusual fatigue or sleepiness.

Inform patients of the signs and symptoms of diabetic ketoacidosis and advise them to seek medical advice immediately if they develop such signs and symptoms.

Stop treatment with SGLT2 inhibitors immediately if diabetic ketoacidosis is suspected or confirmed, and do not re-start treatment unless another clear precipitating factor for the condition is identified and resolved.

Stop treatment with SGLT2 inhibitors temporarily in patients undergoing major surgical procedures or hospitalised due to acute serious medical illnesses. Treatment may be restarted once the patient's condition has stabilised.

3. Local news and GP/pharmacist queries

Query from GP practice:

Switching NOACs

My patient is a 78 year male who is hypertensive with atrial fibrillation. The patient's treatment was changed from warfarin to rivaroxaban as it was difficult to stabilise his INR. A few weeks after starting rivaroxaban the patient has started to complain of severe itching. After two months he can no longer tolerate the itching. Is switching to apixaban a reasonable choice and how can I manage this safely.

Answer:

Firstly urticaria is listed as an "uncommon" (≥ 1/1,000 to < 1/100) side effect of rivaroxaban. As it is a black triangle drug, you should report this side effect (see *below for how to do this).

It's also worth noting that apixaban also lists this as an "uncommon" side effect. There is no guarantee that the patient will be symptom free but worth a trial period.

CKS gives the following advice re switching:

Switching from rivaroxaban or dabigatran to apixaban:

Stop treatment with rivaroxaban or dabigatran and start treatment with apixaban when the next dose of rivaroxaban or dabigatran is due.

For more information, please see this link for local guidance (especially charts - appendices 5 and 6)

*You can report through the Yellow Card website.

For medicines, in some cases you can report using your clinical IT systems, such as the MiDatabank system and SystmOne.

You can send medicines Yellow Card reports by post. Forms are available: by downloading and printing out a form (PDF, 145KB, 2 pages), by writing to FREEPOST YELLOW CARD (no other address details necessary) or by emailing yellowcard@mhra.gsi.gov.uk

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

Quick tips

Before clinicians consider switching patients from one product to another, it would be prudent to check availability of brand through national wholesalers.

Drug name and strength	28 days (or unit cost)	Alternative	28 days (or unit cost)
Aripriprazole 30mg tablets	£114.75	2x15mg	£40.48
Procyclidine	£3.56 (28) but since October concessionary @ £14	Kemadrin	£1.32 (28)
Trazadone	Generic tabs 150mg (28)- £22.75	Molipaxan 150mg	£16.04
	Generic caps 50mg (84)- £25.04	Molipaxan 50mg caps	£23.92

Generic shortages (NCSO and price concessions)

Prescribers should note that the re-imbursement price on FP10 may not necessarily reflect the Drug Tariff price as a result of a drug shortage. These concessionary prices are set by the Department of Health to reflect actual market prices.

A concession only lasts until the end of the month in which it was granted. If there is an on-going supply problem, it is possible that a new concession will be granted by the Department of Health the following month, however this is not guaranteed.

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Drug	Pack size	Drug tariff price	Price concession
Celiprolol 200mg tablets	28	£3.67	£19.83
Celiprolol 400mg tablets	28	£17.79	£39.65
Cimetidine 400mg tablets	60	£7.32	£19.99
Clindamycin 150mg capsules	24	£10.89	£12.49
Ferrous Sulfate 200mg tablets	28	£1.75	£2.85
Lamotrigine 5mg dispersible tablets sugar free	28	£2.69	£7.99
Lercanidipine 10mg tablets	28	£1.48	£5.99
Lercandipine 20mg tablets	28	£1.62	£9.85
Mefenamic acid 500mg tablets	28	£6.44	£10.25
Pioglitazone 30mg tablets	28	£1.31	£34.99
Pioglitazone 45mg tablets	28	£1.47	£39.55
Procyclidine 5mg tablets	28	£3.56	£14.00

UKMI Medicines Compliance Aid Database

The database makes recommendations on the suitability of solid dose forms for transfer from the manufacturers' original packaging to multi-compartment compliance aids (MCAs

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