Derbyshire Medicines Management Newsletter

www.derbyshiremedicinesmanagement.nhs.uk

Volume 7 Issue 3 June 2017

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 vol 55, no. 5, May 2017

Statins: time to rationalise LFTs?

Authors' of an observational comparison of two clinical commissioning groups (CCGs) advocate rationalising the use of liver function tests (LFTs) in people taking statins.

The summary of product characteristics (SPC) list serious liver damage as a rare adverse effect for statin therapy. The National Institute for Health and Care Excellence (NICE) recommends measuring baseline liver transaminase enzymes (alanine aminotransferase or aspartate aminotransferase) before starting a statin and within 3 months of starting treatment and at 12 months, but not again unless clinically indicated. The SPC for simvastatin recommends that LFTs be performed before treatment begins and thereafter when clinically indicated; patients titrated to the 80mg dose should receive an additional test prior to titration, 3 months after titration and periodically thereafter for the first year of treatment.

The observational study included provision of local guidance on monitoring LFTs to one of two London CCGs, while the other received no specific interventions. The intervention group were given access to single alanine transaminase (ALT) test and received advice that a single test on initiation of treatment would suffice, with a single repeat test for those on high-intensity statins.

In the CCG that received the intervention, the promulgation of a local policy and access to a single ALT test resulted in a reduction in the number and total cost of LFT tests. Although, a policy of a single liver function test is not part of NICE's recommendations, it is in line with USA Food and Drug Administration (FDA) drug labelling guidance. The FDA concluded that serious liver injury with statins is rare and unpredictable in individual patients, and that routine periodic monitoring of liver enzymes does not appear to be effective in detecting or preventing serious liver injury. The FDA advises that healthcare professionals should perform liver enzyme tests before initiating statin therapy and as clinically indicated thereafter. A national review of the benefits and harms of a simplified testing regimen for patients taking statins would appear to be warranted.

Prescribers are reminded that the JAPC non-familial hyperlipidaemia guideline recommends baseline LFTs before starting a statin, again at 3 months of starting treatment and at 12 months, but not again unless clinically indicated.

Predictive performance of the CHA2DS2-VASc rule in atrial fibrillation: a systematic review and meta-analysis.
J Thromb Haemost. 2017 Jun;15(6):1065-1077. doi: 10.1111/jth.13690. Epub 2017 May 9.

Van Doorn S, Debray TPA, Kaasenbrood F, Hoes AW, Rutten FH, Moons KGM, Geersing GJ.

The widely recommended CHA2DS2-VASc shows conflicting results in contemporary validation studies. The authors performed a systematic review and meta-analysis of 19 studies validating CHA2DS2-VASc. There was high heterogeneity in stroke risks for different CHA2DS2-VASc scores. This was not explained by differences between setting of care, or by performing meta-regression.

SUMMARY:

The CHA2DS2-VASc decision rule is widely recommended for estimating stroke risk in patients with atrial fibrillation (AF), although validation studies show ambiguous and conflicting results.

Objectives was to:

(i) review existing studies validating CHA2DS2-VASc in AF patients who are not (yet) anticoagulated;
(ii) meta-analyse estimates of stroke risk per score; and
(iii) explore sources of heterogeneity across the validation studies.

The authors performed a systematic literature review and random effects meta-analysis of studies externally validating CHA2DS2-VASc in AF patients not receiving anticoagulants. To explore between-study heterogeneity in stroke risk, they stratified studies to the clinical setting in which patient enrolment started, and performed meta-regression.

In total, 19 studies were evaluated, with over two million person-years of follow-up. In studies recruiting AF patients in hospitals, stroke risks for scores of 0, 1 and 2 were 0.4% (approximate 95% prediction interval [PI] 0.2-3.2%), 1.2% (95% PI 0.1-3.8%), and 2.2% (95% PI 0.03-7.8%), respectively. These were consistently higher than those in studies recruiting patients from the open general population, with risks of 0.2% (95% PI 0.0-0.9%), 0.7% (95% PI 0.3-1.2%) and 1.5% (95% PI 0.4-3.3%) for scores of 0, 1, and 2, respectively. Heterogeneity, as reflected by the wide PIs, could not be fully explained by meta-regression. Conclusions Studies validating CHA2DS2-VASc show high heterogeneity in predicted stroke risks for different scores.
This important systematic review highlights the uncertainty in the appropriate use of a commonly used risk prediction tool. Based on the results of this review, clinicians should be appropriately cautious in their interpretation of the results of CHA2DS2-VASC calculations during shared decision-making with patients.

Pneumococcal vaccines for preventing pneumonia in chronic obstructive pulmonary disease
Cochrane Database Syst Rev Volume 1 , 2017
Walters JA, Tang JN, Poole P, Wood-Baker, R.
People with chronic obstructive pulmonary disease (COPD) are at increased risk of pneumococcal disease, especially pneumonia, as well as acute exacerbations with associated morbidity and healthcare costs the objective of this review was to determine the efficacy of injectable pneumococcal vaccination for preventing pneumonia in persons with COPD.
The review included 12 RCTs involving 2171 participants with COPD (five studies - 606 participants were new). The average age of participants was 66 years, male participants accounted for 67% and mean forced expiratory volume in one second (FEV1) was 1.2 L (five studies), 54% predicted (four studies).
AUTHORS' CONCLUSIONS: Injectable polyvalent pneumococcal vaccination provides significant protection against community-acquired pneumonia, although no evidence indicates that vaccination reduced the risk of confirmed pneumococcal pneumonia, which was a relatively rare event. Vaccination reduced the likelihood of a COPD exacerbation, and moderate-quality evidence suggests the benefits of pneumococcal vaccination in people with COPD. Evidence was insufficient for comparison of different pneumococcal vaccine types.

Sodium-glucose co-transporter-2 inhibitors (SGLT2) and risk of adverse renal outcomes among patients with type 2 diabetes: A network and cumulative meta-analysis of randomized controlled trials
Tang H , Li D , Zhang J , Li Y , Wang T , Zhai S and Song Y .
Diabetes Obes Metab, 2017. https://doi.org/10.1111/dom.12917
This analysis of 58 RCTs (n=38,079) indicates that canagliflozin and dapagliflozin were significantly associated with a greater risk of composite renal events vs placebo, whilst empagliflozin was associated with a lower risk of composite renal events than the control group.
The present meta-analysis indicated that dapagliflozin may increase the risk of adverse renal events, while empagliflozin may have a protective effect among patients with T2DM. Further data from large well-conducted randomized controlled trials and a real-world setting are warranted.
Local guidance places empagliflozin as preferred first line SGLT2 inhibitor and not to initiate if GFR<60ml/min.

Deleted products 2017 | MIMS online for May 2017

Actidose-Aqua (activated charcoal)	Ciloxan Ointment (ciprofloxacin)	Docusol (docusate sodium)
Emadine (emedastine)	Oraldene (hexetidine)	

2. Drug safety update primarily relating to primary care prescribing

(For more information see Drug Safety Update) Volume 10 Issue 10 May 2017

Relevant to Primary Care

Finasteride: rare reports of depression and suicidal thoughts.
The MHRA have received reports of depression and, in rare cases, suicidal thoughts in men taking finasteride 1 mg (Propecia) for male pattern hair loss. Be aware that depression is also associated with finasteride 5 mg (Proscar).
Advice for healthcare professionals:

- since finasteride has been marketed there have been a number of spontaneous adverse drug reaction reports suggesting a possible link to depression, and in rare cases, suicidal thoughts
- advise patients to stop finasteride 1 mg (Propecia) immediately if they develop depression and inform a healthcare professional.
- be aware that the product information for finasteride 5 mg (Proscar) already lists depression as a possible adverse reaction

New CPD e-learning module on reporting suspected adverse drug reactions
MHRA have launched a new free e-learning module to find out more about how and when to report suspected adverse drug reactions and earn CPD credits at the same time

3. Local news and GP/pharmacist queries

Question:
Please could you advice about the risk of dementia in patients taking oxybutynin or similar anti-muscarinic's (anti-cholinergic)?

Answer:
There is a growing body of evidence to support an association between the anticholinergic burden of a patient's treatment regime and an increased risk of dementia and cognitive impairment. The JAPC guidance for the management of overactive bladder recommends the following:

"Antimuscarinic drugs may affect cognitive function in elderly people, hence when prescribing this group of drugs in elderly patients the following should be taken into account:

- In older people being treated for urinary incontinence, every effort should be made to employ non-pharmacological treatments first.
- Use antimuscarinic drugs with caution in elderly patients who are at risk of, or have, cognitive dysfunction.
- In older people who are being prescribed antimuscarinic drugs for control of urinary incontinence, consider modifications to other medications to help reduce anticholinergic load.
- Check mental function in patients on antimuscarinic medication if they are at risk of cognitive dysfunction."

"Oxybutynin immediate release (IR) is the recommended first line treatment choice. Initial dose is up to 5mg bd (start elderly at 2.5mg bd) as long as the patient is reviewed by the Prescriber for side-effects. (NICE CG171 advises not to offer oxybutynin (immediate release) to frail elderly women)."

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

Highlighting potential QIPP opportunities:

Pipexus/Pramipexole SR tablets

Drug tariff price (May 2017)

Strength SR	Pipexus SR cost	Generic Pramipexole SR cost
60mcg x 30	£16.25	£32.49
520mcg x 30	£32.49	£64.98
1.05mg x 30	£64.98	£129.96
1.57mg x 30	£101.18	£202.36
2.10mg x 30	£129.96	£259.91
2.62mg x 30	£168.64	£337.27
3.15mg x 30	£194.94	£389.87

Epact data (May 16 – Apr 17) for Pramipexole SR tabs

CCG	Items	Cost
SDCCG	525	£116,452
ECCG	120	£16,895
NDCCG	520	£76,279
HCCG	378	£46,575
Total	***1,543***	***£256,201***

Pipexus is 50% off the NHS listed price for Pramipexole SR. If the pramipexole had been prescribed as pipexus instead, potentially £128,000 could have been saved.

May

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

Drug Pack	Pack size	Current months Drug tariff price	Price concession
Buspirone 5mg tablets (new)	30	£6.97	£9.95
Buspirone 10mg tablet	30	£3.81	£9.95
Clindamycin 150mg capsules (new)	24	£4.17	£4.85
Dapsone 50mg tablets	28	£41.37	£46.19
Diamorpine 30mg powder for solution for injection ampoules (new)	5	£13.93	£16.52
Ethosuximide 250mg/5ml oral solution	200ml	£4.22	£173.00
Exemestane 25mg tablets	30	£8.00	£12.00
Leflunomide 10mg tablets	30	£5.24	£8.50
Leflunomide 20mg tablets	30	£7.66	£8.50
Lorazepam 1mg tablets	28	£5.26	£6.00
Mefenamic acid 500mg tablets	28	£5.80	£59.99
Mirtazapine 15mg tablets	28	£2.31	£3.00
Mirtazapine 45mg tablets	28	£2.60	£3.00
Nitrofurantoin 100mg tablets	28	£9.85	£11.93
Nitrofurantoin 50mg tablets	28	£14.95	£20.50

	Oxazepam 10mg tablets	28	£3.63	£7.97
	Oxazepam 15mg tablets	28	£2.72	£7.97
	Pramipexole 88 microgram tablets	30	£1.39	£11.24
	Ropinirole 5mg tablets	84	£3.98	£165.00
	Sodium cromoglicate 2% eye drops	13.5ml	£2.35	£5.99
	Spironolactone 50mg tablets	28	£3.16	£5.20
	Tranexamic acid 500mg tablets	60	£4.42	£11.50
	Valsartan 160mg capsules	28	£4.78	£17.10
	Valsartan 40mg capsules	28	£3.44	£8.80
	Valsartan 80mg capsules	28	£3.63	£11.43
	Zolmitriptan 2.5mg tablets	6	£5.06	£14.99
	Zolmitriptan 2.5mg orodispersible tablets SF	6	£1.70	£15.22

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

None 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/
SPS/UKMI Nathnac NHS evidence Electronic medicines compendium Clinical Knowledge Summaries Medicines Prescribing Centre (Formerly NPC) Medicines for children (patient information leaflets Drugs in lactation Medicines Compliance aids Fridge excursions Patent expiries New Medicines	https://www.sps.nhs.uk/ 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 https://www.sps.nhs.uk/?s=&cat%5B%5D=3008 https://www.sps.nhs.uk/?s=&cat%5B%5D=266&cat%5B%5D=3253 https://www.sps.nhs.uk/?s=&cat%5B%5D=3252 https://www.sps.nhs.uk/?s=&cat%5B1%5D=3242 https://www.sps.nhs.uk/category/new-medicines/
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