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 select: 2 February 2017 http://dx.doi.org/10.1136/dtb.2017.2.0453

Statin dosing: morning or evening

A Cochrane review has found that taking a statin in the evening to coincide with cholesterol biosynthesis (chronotherapy) does not confer any additional benefit, in terms of lipid levels, compared with taking it in the morning.

The new review included eight randomised controlled trials of patients with primary or secondary hyperlipidaemia (767 participants) who were assigned to take a statin (lovastatin, simvastatin, fluvastatin or pravastatin) in the morning or in the evening. Trial length varied from 4 to 14 weeks.

Pooled results of secondary outcome analyses demonstrated that chronotherapeutic lipid-lowering regimens had no effect on total cholesterol (mean difference [MD] 4.33mg/dL [0.1mmol/L], 95% CI –1.36 to +10.01), LDL-C (MD 4.85mg/dL [0.13mmol/L], 95% CI –0.87 to +10.57), high-density lipoprotein cholesterol (MD 0.54mg/dL [0.01mmol/L], 95% CI –1.08 to +2.17) or triglycerides (MD –8.91mg/dL [–0.1mmol/L], 95% CI –22.00 to +4.17). There was no difference in adverse events between morning and evening regimens (odds ratio 0.71, 95% CI 0.44 to 1.15). Overall, the quality of the evidence was low because of the risk of methodological bias and imprecision due to wide confidence intervals.

Comment from DTB: The summary of product characteristics for simvastatin tablets and fluvastatin capsules recommend that they are administered in the evening. However, based on the results of the Cochrane review, it may be reasonable to take statins in the morning if concordance with night-time dosing is an issue.

BMJ - (Published 09 March 2017) (Schmidt M, Mansfield KE, et al) doi: https://doi.org/10.1136/bmj.j791

Renal function after new treatment with renin-angiotensin system blockers.

Use of angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) to block action of the renin-angiotensin-aldosterone system is a mainstay of treatment for hypertension, heart failure and diabetic and proteinuric nephropathy, as well as post-myocardial infarction therapy. However, in some patients, renal function declines sharply when they start treatment with these agents. Current guidelines recommend monitoring renal function before and after starting ACEI or ARB and suspending treatment if creatinine concentration increases by more than 30%.

A cohort study undertaken by Schmidt and colleagues (doi:10.1136/bmj.j791) examined the long term cardiorenal outcomes associated with increased concentrations of creatinine after the start of ACEI or ARB treatment. The study used two UK databases—the Clinical Practice Research Datalink and Hospital Episode Statistics—to carry out this population based cohort study. The authors suggest that a 10-30% rise in serum creatinine after the start of treatment can predict increased risk of adverse renal and cardiac outcomes or death, even after correction for baseline renal function. In general, risks were highest in the first year after the start of ACEI/ARB treatment but were sustained up to 10 years later for end stage renal disease, myocardial infarction and death. The study demonstrated a "dose-response" relation between the level of increase in creatinine values and risk of adverse outcome, indicating that all increases below 30% cannot be viewed as safe. The authors conclude that it is not clear whether increases in creatinine values after the start of ACEI/ARB treatment are due to pathophysiological processes representing a biomarker of increased risk or whether a direct causal relation exists between reduced renal function and adverse outcomes.

Prescribers are reminded of the monitoring requirements for ACEI/ARB which can be found in the UKMI Drug monitoring in primary Care for adults. A raised creatinine may be used as a marker to identify patients who need closer monitoring, further cardiovascular risk assessment and lifestyle advice and potentially more aggressive treatment of underlying disorders. However there is a variation to these finding for renal function monitoring in the local Heart failure guidance, which recommends an increase in creatinine up to 50% above baseline as acceptable.

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Health Technology Assessment 2017; Vol. 21: No. 9. https://dx.doi.org/10.3310/hta21090

Oral anticoagulants for primary prevention, treatment and secondary prevention of venous thromboembolic disease, and for prevention of stroke in atrial fibrillation: systematic review, network meta-analysis and cost-effectiveness analysis.

The objective of this health technology assessment was to identify the most effective, safe and cost-effective anticoagulant for stroke prevention in AF and for primary prevention, treatment and secondary prevention of VTE. The authors conducted four systematic reviews, with network meta-analyses of RCTs addressing stroke prevention in AF, primary prevention of VTE, acute treatment of VTE and secondary prevention of VTE.

Conclusions

Novel oral anticoagulants have advantages over warfarin in patients with AF. Of the available NOACs, ***apixaban 5 mg bd offers the best balance between efficacy and safety, and has the highest probability of being most cost-effective***. NOACs offer no efficacy advantage over warfarin in the acute treatment of VTE, but have a lower rate of bleeding complications albeit at a higher cost. For a willingness-to-pay threshold of > £5000, apixaban 5 mg bd emerges as the most cost-effective alternative to warfarin. Neither the clinical effectiveness analysis nor the cost effectiveness analysis provided strong evidence that NOACs should replace post-op LMWH in primary prevention of VTE in patients who are undergoing hip or knee surgery. For treatment of VTE and for preventing repeat venous thromboembolisms, risk of complications due to bleeding was lower for some NOACs than warfarin. Apixaban was the most cost-effective treatment for VTE, but it is not cost-effective to prescribe NOACs or warfarin for preventing recurrence of VTE.

The local AF guidance does not advocate the use of one NOAC over another, instead choice should be guided by clinical and patient factors. However in light of emerging evidence prescribers may want to consider apixaban over the other NOACs for stroke prevention in AF.

Charges for NHS prescriptions, wigs fabric supports and dental care - 1st April 2017

Prescription charges

- Single charge: £8.60
- 3 month PPC (no change): £29.10
- 2 month PPC (no change): £104.00

(Existing arrangements for prescription charge exemptions will remain in place, principally covering those with certain medical conditions like cancer, epilepsy and diabetes, pregnant women and new mothers, children under 16 and anyone over 60, and those on a low income).

Wigs and fabric supports

- Surgical brassiere: £28.40
- Abdominal or spinal support: £42.95
- Stock modacrylic wig: £70.15
- Partial human hair wig: £185.80
- Full bespoke human hair wig: £271.70

Dental charges

- Band 1: £20.60
- Band 2: £56.30
- Band 3: £244.30
- Urgent: £20.60

Deleted products 2016 | MIMS online for November 2016

Arpicolin (procyclidine)	Fersaday (ferrous fumarate)	Sulpor (sulpiride)
Crixivan (indinavir)	Lomont (lofepramine)	Syprol (propranolol)
Zolvera (verapamil)		

2. Drug safety update primarily relating to primary care prescribing

(For more information see Drug Safety Update) Volume 10 Issue 4 November 2016

Not relevant to primary care

- Hyoscine butylbromide (Buscopan) injection: Prescribers are reminded to use hyoscine butylbromide injection with caution in patients with cardiac disease, as the injection can cause serious adverse effects including tachycardia, hypotension and anaphylaxis.

Relevant to primary care

- Yellow card reporting added to second clinical software system. Healthcare professionals are reminded that suspected adverse reactions can be reported to MHRA directly through their clinical software (this now includes SystmOne and Vision)

Other safety news…

Safe use of Braltus delivered via a zonda inhaler

For some time Spiriva (Handihaler) has been the only brand of dry powder tiotropium available on the market. However, recently a new brand of this medication has been released, called Braltus. Braltus contains the same ingredient (tiotropium) but the device is very slightly different from the Handihaler, but it works in essentially the same way. As Braltus is available at a lower cost to the NHS, the Derbyshire CCGs (including Erewash CCG) have decided to switch patients from the Spiriva brand to Braltus.

Healthcare professionals are reminded of the key points for Braltus inhaler:

- Please advise patients NEVER to insert the capsule directly into the mouthpiece, always follow the instructions provided with the inhaler.
- Braltus capsules are in a pot rather than a blister pack.
- Braltus capsules are transparent so it is easier to see if the full dose has been inhaled.
- The delivered dose of Braltus and Spiriva is the same:
  - Tiotropium (Braltus) is described on the clinical system as being a 10mcg dose. Each capsule contains 16 micrograms of tiotropium bromide (the salt), equivalent to 13micrograms of tiotropium, but the delivered dose (the dose that leaves the mouthpiece of the Zonda® device) is 10micrograms.
  - Tiotropium (Spiriva) is described on the clinical system as being an 18mcg dose. Each capsule contains 22.5 microgram tiotropium bromide monohydrate (the salt) equivalent to 18microgram tiotropium. The delivered dose (the dose that leaves the mouthpiece of the HandiHaler® device) is 10micrograms.
- The patient will receive a new Zonda inhaler device each month and are asked to safely dispose of the old one. This means that patients do not need to clean their Zonda device.
- The devices are not interchangeable - tiotropium capsules (Spiriva) are not to be used in the Zonda inhaler and vice versa.

Lucozade® energy is changing

Reduction in sugar content of Lucozade – implications for Oral Glucose Tolerance Test (OGGT) & treatment of Hypoglycaemia

As we are all aware, the government has announced two main measures to reduce the sugar content in our food and drinks. The first is the Sugary Drinks Industry Levy (SDIL) sometimes called the 'sugar tax.' This Levy will charge soft drink manufacturers for producing soft drinks that are high in added sugar. The aim of this is to encourage the soft drink industry to change their recipes to reduce the sugar content in their drinks to avoid the added charge. It will come into force in April 2018. The second is the sugar reduction programme, which is being run by Public Health England. Its aim is to reduce the amount of sugar in foods by 20 per cent by 2020. This focuses on the food products most commonly eaten by children, so things like sweets, chocolate, yoghurts and biscuits to name just a few. The work on this is underway.

The manufacturers of Lucozade® have chosen to reduce the sugar content of their products so that they will now contain approximately 50% fewer glucose based carbohydrates than before. This means that patients are likely to need to drink more if/when using this product to treat a hypo. New products will appear on shelves from April 2017, so it is possible that old and new recipes may appear on the shelf at the same time. Therefore, it is vital that patients check the label on the product before using it as a hypo treatment to ensure they drink the required amount to correct the hypo.

Some Outpatient clinics or GP practices may perform Oral Glucose Tolerance Tests (OGTT) using Lucozade® products; therefore they will need to review their current practice & policies in light of this upcoming change in sugar content of Lucozade® and other products in the future. The choice of whether to reduce the sugar content in products is down to the companies themselves. This will mean different companies will respond in different ways and at difference speeds. They may not always publicise when they have reduced the sugar content either.
So it is imperative that you check the product that you use in a clinical setting before use, to ensure you are using enough. Alternatively, you could use a suitable prescribed product.

Further information for patients and healthcare professionals can be found on the Diabetes UK and Lucozade websites.

Nutritional information for Lucozade®

Typical values	100ml	380ml
Energy : kJ/kcal	158/37	600/141
Carbohydrate, g	**8.9**	**33.8**
of which sugars, g	4.5	17.1
Salt, g	0.08	0.31

Contains negligible amounts of – Fat, saturates and protein

Contains 8.9g glucose based carbohydrate per 100ml and 33.8g per 380ml bottle.

(Reference intake of an average adult (8400kJ/2000kcal))

Information from Diabetes UK:

If a patient has been advised to drink Lucozade® Energy Original when their blood glucose is low, the amount they drink will need to change. For example if they have been told they need:

- 10g of carbohydrate, they will need 110ml
- 15g of carbohydrate, they will need 170ml

3. Local news and GP/pharmacist queries

Query from non-dispensing GP practice:

Q: What should we advise patients to do when they bring back unwanted medicines, dressings, and sharps waste to the GP Surgery?

A: All pharmacies are obliged to accept unwanted medicines from patients, including dressings and medicines considered as hazardous (e.g. hormonal preparations, oral cytotoxic medicines etc.) as an essential service under the national Pharmacy Contract. Patients presenting at a non-dispensing GP practice with such items should be asked to return them to their local pharmacy for disposal. This also applies to patients in a residential home, however nursing homes providing nursing care to patients are required to make their own waste disposal arrangements. Dispensing practices are obliged to accept unwanted medicines from those patients that they dispense for.

Pharmacies are not able to accept sharps waste from patients e.g. insulin needles or medicines contained in pre-filled syringes etc. Patients who are prescribed such items should also be provided with a sharps bin and be instructed in how to use it safely and where to return it when full. Patients prescribed insulin needles and other items requiring disposal in a sharps bin in primary care should be prescribed an appropriate sharps bin on prescription and be advised to return to their GP practice when full. N.B. North Derbyshire CCG commissions a home care delivery service for patients prescribed methotrexate pre-filled syringes under a shared care arrangement.

A joint Derby and Derbyshire sharps collection service for housebound patients is available see link below
http://www.derby.gov.uk/environment-and-planning/recycling-rubbish-and-waste/clinical-household-waste/

Covert administration of medicines

Covert administration of medicines is a complex issue and involves disguising the administration of a medicine (e.g. in food or drink) to a patient lacking the mental capacity to consent to treatment. Specialist Pharmacy Services (SPS) have produced a Q&A document discussing some of the legal issues that need to be considered before medicines are given covertly. It also addresses some of the pharmaceutical issues (e.g. absorption, incompatibility, interactions) and patient factors (e.g. acceptability) that need to be considered when deciding whether to administer medicines in this way.

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

Generic vs brand

A generic medicine contains the same quantity of active substance(s) as the branded medicine.

- Generic medicines are, overall, much less expensive to the NHS. Their appropriate use instead of branded medicines delivers considerable cost savings.

Epact data for Feb 2016- Jan 2017

Prescriber	Preparation	Items	Cost
ECCG	Losec caps 10mg, 20mg, 40mg	151	£3,757
HCCG	Losec caps 10mg, 20mg, 40mg	133	£1,937
NDCCG	Losec caps 10mg, 20mg, 40mg	748	£15,664
SDCCG	Losec caps 10mg, 20mg, 40mg	980	£28,340
	Total	1960	£56,680

Comparing cost of losec capsules with omeprazole caps

Preparation	Omeprazole caps	Losec capsules
10mg	89p x28	£7.75 x 28
20mg	91p x 28	£11.60 x 28
40mg	75p x 7	£5.80 x 7

Prescribers are reminded that prescriptions should be written generically unless there is a cost or clinical reason not to do so. A list of items that should be prescribed by brand name for patient safety reasons can be found in appendix 2 of Guidance on Prescribing in Primary Care.

There may be certain circumstances when it may be appropriate to specify the branded medicine. These include:

- Drugs with a narrow therapeutic index
- Certain modified or controlled release drugs
- Certain administration devices
- Multiple ingredient products
- 'Biosimilar' medicines
- Ensuring adherence to long-term medications, where differences in appearance between manufacturer's products might cause confusion and anxiety

Reminder of cost effective alternatives included in the Derbyshire formulary:

1. Peptac sugar-free suspension - 1st line. Acidex Advance suspension - lower Na+ concentration than peptic, but costs considerably more than peptac.

February

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
Amitriptyline 50mg tablets	28	£2.77	£3.50
Buspirone 5mg tablets (new)	30	£3.19	£17.50
Candesartan 2mg tablets	7	£1.92	£2.25
Dapsone 50mg tablets	28	£40.77	£46.19
Exemestane 25mg tablets	30	£5.71	£12.60
Flecainide 100mg tablets	60	£10.10	£16.53
Flecainide 50mg tablets	60	£8.64	£11.57
Glibenclamide 5mg tablets	28	£1.39	£2.49
Leflunomide 10mg tablets (new)	30	£4.69	£7.79
Leflunomide 20mg tablets (new)	30	£4.62	£9.03
Lorazepam 1mg tablets	28	£4.41	£5.71
Mirtazapine 15mg tablets	28	£1.19	£5.45
Mirtazapine 30mg tablets	28	£1.27	£1.61
Mirtazapine 45mg tablets	28	£1.55	£5.95
Naratriptan 2.5mg tablets	6	£4.21	£23.00
Nitrofurantoin 100mg tablets	28	£7.03	£16.80
Nitrofurantoin 50mg tablets	28	£11.66	£17.50
Oxazepam 10mg tablets	28	£1.37	£7.97
Oxazepam 15mg tablets	28	£1.38	£7.97
Ropinirole 0.5mg tablets	28	£13.63	£15.50
Ropinirole 1mg tablets	84	£2.07	£56.71
Ropinirole 2mg tablets	28	£2.80	£22.25
Ropinirole 5mg tablets	84	£3.91	£165.00
Spironolactone 50mg tablets	28	£1.70	£5.20
Valsartan 160mg capsules	28	£4.05	£5.20
Valsartan 40mg capsules (new)	28	£3.31	£4.72
Valsartan 80mg capsules (new)	28	£2.21	£5.55
Zolmitriptan 2.5mg tablets	6	£1.48	£15.30

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/
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