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 Vol 55 no. 9 September 2017 http://dtb.bmj.com/content/55/9#Articles

European guideline on antimicrobial resistance

The European Commission (EC) has highlighted the need for prudent use of antimicrobials in human health. The EC recognises that ultimate responsibility for the prudent use of antimicrobials lies with national, regional or local governments.

Many elements of the guidance already form part of UK antimicrobial stewardship activities. The key recommendations underpin the core principle that careful assessment and judicious use of antimicrobials are paramount to reduce the burden of antimicrobial resistance. To this end, the Royal College of General Practitioners' 'TARGET' toolkit (advocated for local use in primary care) reinforce many of the key messages.

Link is included to the EC document: https://ec.europa.eu/health/amr/sites/amr/files/amr_guidelines_prudent_use_en.pdf

Diagnosis and investigations of fungal skin and nail infections

NHS England has issued a re-formatted quick reference guide on the diagnosis and treatment of fungal skin and nail infections. Aimed at primary care prescribers in general practice and out-of-hours settings, including doctors, nurses and pharmacists, the guide's stated intentions are to "provide a simple, effective, economical and empirical approach to the diagnosis and treatment of fungal skin and nail infections [and] to minimise the emergence of antibiotic resistance in the community."

Comment: Complications of fungal nail infection are uncommon but can include secondary bacterial infections and cellulitis, especially in patients who have underlying vascular disease, diabetes or connective tissue disorders. This guide provides a useful reminder of what constitutes best practice in the diagnosis, investigation and management of fungal skin and nail infections.

Link is included to the PHE document:
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/619770/Fungal_skin_and_nail_infections_guidance.pdf

Value of SMBG in non-insulin-treated type 2 diabetes

The value of self-monitoring of blood glucose (SMBG) levels in patients with non-insulin-treated type 2 diabetes in primary care has been assessed in an open-label randomised trial..

Primary outcomes were improvement in glycated haemoglobin (HbA1c) level and health-related quality of life (HRQOL). A total of 450 patients, were randomised to one of three interventions:

- no SMBG;
- standard once-daily SMBG consisting of glucose values immediately reported to the patient through the blood glucose meter; or
- enhanced once-daily SMBG consisting of glucose values immediately reported to the patient plus automated, tailored messages. Messages were intended to educate and motivate.

The authors found no significant differences in HbA1c levels or HRQOL across all three groups.

Local type 2 diabetes guidance based on NICE NG28 states do not routinely offer SMBG for adults with type 2 diabetes unless:

- *the person is on insulin or*
- *there is evidence of hypoglycaemic episodes or*
- *the person is on oral medication that may increase their risk of hypoglycaemia while driving or operating machinery or*
- *the person is pregnant, or is planning to become pregnant.*

Vortioxetine for acute depression in adults

Vortioxetine is from a new class of psychotropic drugs that acts on the serotonin system. It is licensed for the treatment of major depression in adults. A Cochrane review has assessed the efficacy and acceptability of vortioxetine compared with placebo and other antidepressant drugs in the treatment of acute depression in adults.

The review's authors suggested that vortioxetine may be more effective than placebo across three efficacy outcomes of response, remission and depressive symptoms.

DTB comment: Vortioxetine is a thirdline option for treating major depressive episodes in adults. The Cochrane reviewers suggested that the place of vortioxetine in the treatment of acute depression is **unclear** and that the clinical relevance of its effect in terms of response, remission and depressive symptoms compared with placebo is uncertain. Of particular concern was the lack of studies comparing vortioxetine with SSRIs, the small number and poor quality of studies comparing it against any other antidepressants and the questionable clinical importance of its modest performance against placebo.

Locally vortioxetine has been classified a RED as per NICE TA367 for treating major depressive episodes; requiring specialist assessment to enable patient selection, initiation and on-going treatment.

Managing Scarlet fever
Scarlet fever is usually a mild self-limiting illness caused by Streptococcus pyogenes (group A streptococcus [GAS]), characterised by non-specific symptoms such as sore throat early in illness before the typical rash develops. It can, rarely, lead to severe and even fatal complications. There has been a rise in notifications of scarlet fever in recent years in several countries, including the UK.
If scarlet fever is suspected or confirmed, general management may include rest, fluids, paracetamol and patients should be advised about good hygiene measures to reduce the risk of transmission. There are few UK guidelines specifically addressing the management of scarlet fever and little published evidence on the effectiveness of antibiotic therapy. Advice from Public Health England advocates the use of antibiotics for scarlet fever to minimise the risk of onward transmission and complications.

Why and how to step down chronic asthma drugs http://www.bmj.com/content/bmj/359/bmj.j4438.full.pdf
Gionfriddo M, Hagna JB, Rank MA. BMJ 2017;359:J4438
This article reviews the evidence for stepping down chronic asthma drugs. The goal of asthma management is to control symptoms while minimizing the side effects of treatment. Step-down has been studied for several types of asthma drug regimens, and certain approaches may have lower risk than others. Systematic reviews of multiple trials support the following specific step-down approaches:

- optimizing inhaled corticosteroid dosing when stepping down oral corticosteroid,
- reducing inhaled corticosteroid from a higher dose,
- lowering inhaled corticosteroid-long acting bronchodilator (ICS-LABA) dose while adding ICS-LABA on-demand,
- adding leukotriene receptor antagonist while lowering inhaled corticosteroid dose,
- and using allergen immunotherapy when reducing inhaled corticosteroid from a higher dose.

The local asthma guidance for adults and children is currently under review and will be updated in line with the publication of NICE guidance.

Deleted products 2017 | MIMS online for September 2017

Lescol Capsules (fluvastatin)	Teoptic (carteolol)	Altargo (retapamulin)

2. Drug safety update primarily relating to primary care prescribing

(For more information see Drug Safety Update) Volume 11 Issue 2 September 2017

Guidance on the use of adrenaline auto-injectors in schools, Sep 2017
From the 1st October 2017 the Human Medicines Regulations 2017, will allow all schools to buy adrenaline auto-injector (AAI) devices without a prescription, for emergency use in children who are at risk of anaphylaxis but their own device is not available or not working (e.g. because it is broken or out-of-date). The Department of health have issued new guidance for schools on how to use AAIs as well as how to spot the signs of a mild allergic reaction and severe anaphylaxis, and how best to respond.

https://www.gov.uk/government/publications/using-emergency-adrenaline-auto-injectors-in-schools

Miconazole (Daktarin): over-the-counter oral gel contraindicated in patients taking warfarin
Patients taking warfarin should not use over-the-counter miconazole oral gel (Daktarin). If you plan to prescribe miconazole oral gel in a patient on warfarin, you should closely monitor them and advise that if they experience any sign of bleeding, they should stop miconazole oral gel and seek immediate medical attention.
Advice for healthcare professionals:

- bleeding events, some with fatal outcome, have been reported with use of miconazole oral gel by patients on warfarin
- patients taking warfarin should not use over-the-counter miconazole oral gel available from pharmacies
- if the concomitant use of miconazole oral gel with an oral anticoagulant such as warfarin is planned, exercise caution and ensure that you monitor and titrate the anticoagulant effect carefully
- advise patients taking prescription-only miconazole oral gel and warfarin that if they experience signs of over-anticoagulation, such as sudden unexplained bruising, nosebleeds, or blood in urine, they should stop using miconazole and seek immediate medical attention

Loperamide (Imodium): reports of serious cardiac adverse reactions with high doses of loperamide associated with abuse or misuse
There have been reports of cardiac events including QT prolongation, torsades de pointes, and cardiac arrest in patients who have taken high or very high doses of loperamide as a drug of abuse or for self-treatment of opioid withdrawal.
Advice for healthcare professionals:

- Serious cardiovascular events (such as QT prolongation, torsades de pointes, and cardiac arrest), including fatalities, have been reported in association with large overdoses of loperamide. (In the region of 400-800mg)
- healthcare professionals are reminded that if symptoms of overdose occur, naloxone can be given as an antidote
- Since the duration of action of loperamide is longer than that of naloxone (1–3 hours), repeated treatment with naloxone might be indicated; patients should be monitored closely for at least 48 hours to detect possible CNS depression.
- As for all medicines, pharmacists should remind patients not to take more than the recommended dose on the label.
- Report all suspected adverse reactions, including those associated with abuse or misuse, to the Yellow Card Scheme.

Learning from Medication Errors/Incidents
Incorrect dose of Atomoxetine prescribed and dispensed (during cyber-attack, May 2017) – prescriber unable to access clinical systems during a recent cyber-attack.
An incident has been reported locally that occurred during the cyber-attack earlier this year, which left GP practices without access to their clinical systems. An 8 year old patient required a repeat prescription for atomoxetine as they had run out of their supply. As the Nurse Prescriber (NP) was unsure of the dose that the patient was taking and couldn't access patient records, they contacted their community pharmacy to check (from past dispensed items on this patient's record).

The NP understood the dose to be communicated over the phone as 80mg; however the correct dose was 18mg. The error was identified when the notes were being added onto the clinical system the following week and had not been identified by the community pharmacy at the point of dispensing. It was discovered that the patient had received around 7 days of the incorrect dose and required a check-up at the Children's Emergency Department to ensure that no harm had occurred to the patient.

Both the GP Practice and Community Pharmacy have been carrying out their own internal investigations.

In order to reduce the risk of such incidents occurring again, GP practices are encouraged to consider the following key points:

1) Systems and processes must be in place to effectively deal with loss of access to Clinical Systems – have a business continuity plan in place.

2) Ensure clearer communication over the telephone – especially when medication doses, strengths or volumes are being checked or confirmed. Good practice points include:

   (i) Repeating what you have heard over the phone and confirming your understanding of the information received.

   (ii) Communicating information around doses, strengths or volumes of medication more specifically– especially when there is a risk that they could sound alike e.g. 18 vs. 80. Instead of stating '18' or '80', communicate by saying "do you mean 'one eight'"? Or 'eight zero'? This equally applies to you if you are providing such information to others.

3. Local news/selfcare and GP/pharmacist queries

GP QUERY

Question:
Can NOACs/ DOACs be used for someone who has a porcine valve? The guidance only mentions mechanical valves.

Answer:
There are different types of heart valves: mechanical valves which are also known as mechanical prosthetic valves or prosthetic valves and tissue valves which are also called biological valves or bioprosthetic heart valves which is the type of valve a prosthetic porcine valve falls under.

Patients with mechanical heart valves require life-long anticoagulation with a vitamin K antagonist, i.e. warfarin guided by regular INR monitoring. At present, there are no published randomised controlled trials that have evaluated the efficacy and safety of the new novel oral anticoagulants (NOAC) or direct oral anticoagulants (DOAC) as they are now called (e.g. Dabigatran, Rivaroxaban, Apixaban, etc) in patients with prosthetic heart valves. As a result, no data are available suggesting that they provide adequate anticoagulation in patients with mechanical prosthetic heart valves. The use of NOACs in this group of patients is therefore not licensed and is contra-indicated until further information becomes available. This warning is clearly indicated in the products' Summary of Product Characteristics and the Updated European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist anticoagulants in patients with non-valvular atrial fibrillation.

Valvular indications and contraindications for NOAC therapy in AF patients

	Eligible	Contra-indicated
Mechanical prosthetic valve		✓
Moderate to severe mitral stenosis (usually of rheumatic origin		✓
Mild to moderate other native valvular disease	✓	
Severe aortic stenosis	✓ Limited data. Most will undergo intervention	
Bioprosthetic valve[a]	✓ (except for the first 3 months post-operatively)	
Mitral valve repair[a]	✓ (except for the first 3–6 months post-operatively)	
PTAV and TAVI	✓ (but no prospective data; may require combination with single or double antiplatelets: consider bleeding risk)	
Hypertrophic cardiomyopathy	✓ (but no prospective data)	

PTAV, percutaneous transluminal aortic valvuloplasty; TAVI, transcatheter aortic valve implantation.
[a]American guidelines do not recommend NOAC in patients with biological heart valves or after valve repair.

Adapted from Updated European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist anticoagulants in patients with non-valvular atrial fibrillation - Europace (2015) 17, 1467–1507 doi:10.1093/europace/euv309

From the above table (taken from the European Heart Rhythm Association Practical Guide) the guide states that atrial fibrillation patients with bioprosthetic valves constitute a grey area as some of these patients were included in some trials on non-valvular AF and so they may be suitable candidates. However there is an exclusion such that the NOACs should not be started 3 months post-operatively in these patients.

Overall, NOACs including rivaroxaban are contra-indicated in patients with mechanical prosthetic valves, but can be used in patients with bioprosthetic heart valves (so porcine valves in your query) but not within 3 months post-op of the valve replacement.

Withdrawal of Bovine Insulin: Guidance for Healthcare Professionals - Diabetes UK

Bovine insulin preparations will be withdrawn from the end of 2017 due to limited availability of the active ingredient. The predicted stock depletion is as follows:

Description	Form	Predicted depletion date
Hypurin® Bovine Isophane	3ml Cartridges	December 2017 (Product Expiry)
Hypurin® Bovine Neutral	3ml Cartridges	June 2018
Hypurin® Bovine Neutral	10ml Vial	July 2018
Hypurin® Bovine Isophane	10ml Vial	December 2018
Hypurin® Bovine Lente (IZS)	10ml Vial	May 2019 (Product Expiry)
Hypurin® Bovine PZI	10ml Vial	August 2019

People with insulin-treated diabetes using bovine insulin preparations will continue to require insulin treatment so will need to be changed to alternative, acceptable insulin preparations.

For further details regarding changing of bovine insulin see: https://www.diabetes.org.uk/resources-s3/2017-10/Insert_Fact-File-32_SA6_HR.pdf

Summary
Bovine insulin's are being withdrawn and all patients still using these insulin's will need to change to different insulin's. They are a vulnerable group and the change is likely to be challenging with a high risk of hypoglycaemia and glucose instability. The change will require considerable education of patients, families and carers and careful follow up. **Diabetes specialist multidisciplinary team supervision is essential.**

Movelat – PrescQIPP message
It has come to our attention that there have been some challenges to commissioners from the Movelat representatives around the "incorrect classification" of Movelat as a rubefacient. At least one CCG, to our knowledge has received a legal letter on this topic, and we anticipate that more may follow. Firstly, if you have received a formal challenge or complaint we'd be keen to know so we can build a picture on this. We have also flagged to NHS E and NHSCC to raise awareness.

PrescQIPP have also had several communications with the company around this. Originally it was classed as a rubefacient in the BNF and in Cochrane reviews. The company have recently had the product classified by the MHRA as M02AC (topical products for joint and muscular pain - preparations with salicylic acid derivatives) and feel that this means the product is no longer a rubefacient and is an anti-inflammatory product. Other products in this category include Ralgex Muscle Rub, which is a rubefacient.

Topical NSAIDS have the classification M02AA (Anti-inflammatory preparations, non-steroids for topical use). We have therefore responded to the company to let them know we will not be changing our bulletin and still consider Movelat to be a rubefacient

All rubefacients are classified as BLACK by JAPC for Derbyshire – not recommended for prescribing.

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

Highlighting potential QIPP opportunities:
Following a recent decision by JAPC, prescribers are reminds that **Vitamin D 800units** for maintenance treatment following treatment of deficiency or insufficiency (excluding patients with osteoporosis, osteopenia or primary hyperparathyroidism), are classified as **BLACK** – not routinely recommended or commissioned. Prescribers should encourage patients to make lifestyle changes and to purchase a supplement over the counter from a local pharmacy, health food shop or supermarket. For further details see position statement for self-care with Vitamin D , local vitamin D guidance and patient information leaflet regarding maintenance of Vit D levels.

September
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 size	Price concession	Drug tariff price
Anastrozole 1mg tablets	28	£14.45	£1.00
Atorvastatin 80mg tablets	28	£2.20	£1.65
Buspirone 10mg tablets	30	£9.00	£5.28
Chlorpromazine 25mg tablets	28	£32.20	£1.62

Chlorpromazine 100mg tablets	28	£35.00	£1.65
Citalopram 10mg tablets	28	£1.58	£0.66
Citalopram 20mg tablets	28	£2.30	£0.71
Citalopram 40mg tablets	28	£2.60	£0.81
Diamorphine 30mg powder ampoules	5	£16.52	£12.13
Gabapentin 300mg capsules	100	£13.95	£2.36
Hydroxychloroquine 200mg tablets	60	£16.50	£3.04
Levetiracetam 1g tablets	60	£92.50	£4.70
Levetiracetam 250mg tablets	60	£27.50	£2.06
Levetiracetam 500mg tablets	60	£49.32	£2.17
Mefenamic acid 500mg tablets	28	£55.00	£5.35
Nitrofurantoin 100mg tablets	28	£12.00	£9.07
Olanzapine 10mg tablets	28	£65.00	£0.98
Olanzapine 15mg tablets	28	£84.50	£1.27
Olanzapine 2.5mg tablets	28	£16.49	£0.92
Olanzapine 20mg tablets	28	£108.99	£1.38
Olanzapine 5mg tablets	28	£32.25	£0.92
Olanzapine 7.5mg tablets	28	£52.44	£1.00
Oxazepam 10mg tablets	28	£18.49	£4.46
Oxazepam 15mg tablets	28	£18.49	£4.33
Pramipexole 88mcg tablets	30	£13.50	£2.06
Quetiapine 100mg tablets	60	£70.00	£1.36
Quetiapine 150mg tablets	60	£72.00	£1.87
Quetiapine 200mg tablets	60	£71.00	£2.14
Quetiapine 25mg tablets	60	£24.95	£0.93
Rasagiline 1mg tablets	28	£13.95	£1.59
Rizatriptan 10mg tablets	3	£13.37	£1.44
Sodium cromoglicate 2% eye drops	13.5ml	£9.72	£2.08
Sumatriptan 100mg tablets	6	£22.00	£1.32
Sumatriptan 50mg tablets	6	£15.00	£1.29
Terbinafine 250mg tablets	14	£12.49	£1.16
Trimethoprim 50mg/5ml Oral Susp SF	100ml	£3.99	£1.39
Valsartan 160mg capsules	28	£14.95	£4.66
Valsartan 40mg capsules	28	£5.37	£5.37
Valsartan 80mg capsules	28	£11.43	£5.63
Vitamin B Co Strong tablets	28	£5.50	£1.32
Zolmitriptan 2.5mg orodispersible tablets SF	6	£18.27	£4.53
Zolmitriptan 2.5mg tablets	6	£18.00	£8.56

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

NG73: Endometriosis – diagnosis and management.
This guideline covers diagnosing and managing endometriosis. It aims to raise awareness of the symptoms of endometriosis, and to provide clear advice on what action to take when women with signs and symptoms first present in healthcare settings. It also provides advice on the range of treatments available.

PH38: Type 2 diabetes prevention in people at high risk.
This guideline covers how to identify adults at high risk of type 2 diabetes. It aims to remind practitioners that age is no barrier to being at high risk of, or developing, the condition. It also aims to help them provide those at high risk with an effective and appropriate intensive lifestyle-change programme and metformin to prevent or delay the onset of type 2 diabetes.

6. Useful resources

BMJ	www.thebmj.com
JAMA: The Journal of the American Medical Association	http://jama.ama-assn.org/
Drugs and Therapeutic Bulletin "Full access to articles available to SDCCG clinicians"	http://dtb.bmj.com/
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