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 3. March 2017

Penicillin allergy – getting the label right

Penicillin allergy is an immunologically mediated hypersensitivity reaction that can be life-threatening. However many patients who have been recorded as being penicillin-allergic may have had a non-immunological adverse effect (e.g. vomiting, diarrhoea and non-specific rash), an idiopathic reaction or other temporally-related adverse reaction that was inappropriately attributed to the drug.

Ensuring that a documented record of penicillin allergy is correctly used has benefits for patients and may reduce healthcare costs and antibacterial resistance. Penicillin's should be withheld from people with a documented allergy to penicillin. Patients who are likely to require frequent treatment with a penicillin or treatment with a specific penicillin in the future should be considered for referral to specialist allergy clinics for confirmation or exclusion of penicillin allergy. Cross-reactivity to other beta-lactams (e.g. cephalosporins that have the same or similar side chains in their molecular structure) can occur. People who have experienced minor reactions to penicillin's that have been incorrectly recorded as an allergic response may be able to tolerate second and third generation cephalosporins, carbapenems or monobactams. Non-beta-lactam antibacterials are an alternative in those with proven penicillin allergy or those at high risk of severe or life-threatening reactions.

DTB recommends that for those patients with a documented record (allergy status) of penicillin allergy, clear communication between healthcare professionals and across healthcare organisations is required to avoid the adverse consequences of allergic reactions (where there is a true allergy to penicillin) or unnecessary use of alternative antibacterials (in cases where the patient had previously experienced side effects).

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Potential for abuse and misuse of pregabalin and gabapentin

The Advisory Council on the Misuse of Drugs (ACMD) has highlighted concerns over the misuse of pregabalin and gabapentin. The chair of the ACMD has written to the UK government to request that pregabalin and gabapentin be classed as controlled drugs

The ACMD conducted a review of the potential harms associated with the misuse of these drugs. It noted that in the UK, prescribing of pregabalin and gabapentin has increased by 350% and 150% respectively over 5 years. UK survey data suggests that abuse of pregabalin and gabapentin is common among opioid-using and prison populations.

Prescribers are reminded of the PHE advice issued in 2014 on the risk of misuse of pregabalin and gabapentin, and suggestions for a balanced and rational use of these medicines. Locally pregabalin has a green classification for epilepsy after specialist initiation and neuropathic pain; and green after specialist initiation for generalised anxiety disorder where SSRIs or venlafaxine are ineffective, poorly tolerated or considered clinically inappropriate. Gabapentin is classified as green after consultant/specialist initiation for epilepsy

Current prescribing across Derbyshire for the previous 12 months:

- Gabapentin 142,877 items at a cost of £614,648
- Pregabalin 67,353 items at a cost of £4,198,202

**See also further medication safety related news for pregabablin and gabapentin in the Drug Safety section below*.*

Pneumonia risk in asthma patients using inhaled corticosteroids: a quasi-cohort study

Qian CJ, Coulombe J, Suissa S, Ernst P. Br J Clin Pharm. 7 May 2017. DOI: 10.1111/bcp.13295

A cohort study looked at 152 412 asthma subjects who had previously been exposed to an inhaled corticosteroid (ICS) within the past 60 days prior to their pneumonia index event or matched person-moment. The study found there was an increased risk of pneumonia associated with current use of ICS (RR1.83; 95%CI:1.57- 2.14) or an excess risk of 1.44 cases per 1000 person-years (RD 1.44; 95% CI 1.03 - 1.85).

There was an excess pneumonia risk with low doses (RR 1.60; 95% CI 1.06, 2.45), moderate doses (RR 1.53; 95% CI 1.12, 2.08) and high doses (RR 1.96; 95% CI 1.64, 2.34) of ICSs, and with budesonide (RR 2.67; 95% CI 2.05, 3.49) and fluticasone (RR 1.93; 95% CI 1.58, 2.36), specifically relative to no use. When accounting for potential protopathic bias, the risk with current use of ICSs was attenuated (RR 1.48; 95% CI 1.22, 1.78). The study concluded that ICS use in asthma patients appears to be associated with an increased risk of pneumonia and is present for both budesonide and fluticasone.

Prescribers are reminded that:

- It is important to monitor therapy regularly and titrate down to the lowest dose at which effective control of asthma is maintained.
- Growth (height and weight centile) should be monitored at least annually in children with asthma.
- If a doctor considers that a child's asthma is not controlled on the maximum licensed dose of their inhaled corticosteroid, despite the addition of other therapies, the child should be referred to a specialist in the management of paediatric asthma.

Novel oral anticoagulants compared to warfarin for atrial fibrillation and venous thromboembolism: systematic review, network meta-analysis and cost-effectiveness analysis

HTA Volume: 21, Issue:9, Published in March 2017

The objective was to determine the best oral anticoagulant/s for prevention of stroke in AF and for primary prevention, treatment and secondary prevention of VTE.

The review found that NOACs have advantages over warfarin in AF patients, but there was no strong evidence they should replace warfarin/low molecular weight heparin in primary prevention (PV), treatment or secondary prevention of venous thromboembolism. Findings limited by lack of head to head NOAC studies.

Early non-persistence with dabigatran and rivaroxaban in patients with atrial fibrillation.

Jackevicius CA, Tsadok MA, Essebag V, Atzema C, Eisenberg MJ et al. Heart, March 2017

DOI 10.1136/heartjnl-2016-310672

Dabigatran and rivaroxaban are novel oral anticoagulants (NOACs) approved for stroke prevention in atrial fibrillation (AF). Although NOACs are more convenient than warfarin, their lack of monitoring may predispose patients to non-persistence. Limited information is available on NOAC non-persistence rates and related clinical outcomes in clinical practice.

A retrospective cohort study using administrative data from Ontario, Canada, from January 1998 to March 2014 of patients with AF who were dispensed dabigatran or rivaroxaban was undertaken. Non-persistence was defined as a gap in dabigatran or rivaroxaban prescriptions ≥14 days. The primary composite outcome was stroke, transient ischaemic attack (TIA) and mortality associated with non-persistence.

Results from the cohort study found at 6 months, 36.4% of patients were non-persistent to dabigatran, while 31.9% of patients were non-persistent to rivaroxaban. Stroke/TIA/death was significantly higher for those non-persistent to dabigatran (HR 1.76 (95% CI 1.60 to 1.94); p<0.0001) or rivaroxaban (HR 1.89 (95% CI 1.64 to 2.19); p<0.0001) compared with those who were persistent. Risk of stroke/TIA was markedly higher in non-persistent patients to dabigatran (HR 3.75 (95% CI 2.59 to 5.43); p<0.0001) and rivaroxaban (HR 6.25 (95% CI 3.37 to 11.58); p<0.0001) than those persistent.

The study concluded NOAC non-persistence rates are high in clinical practice, with approximately one in three patients becoming non-persistent to dabigatran or rivaroxaban within 6 months after drug initiation. Non-persistence with either dabigatran or rivaroxaban is significantly associated with worse clinical outcomes of stroke/TIA/death.

NSAIDs and risk of cardiac arrest

Danish Registry study found use of diclofenac (OR, 1.50; 95% CI, 1.23–1.82) and ibuprofen (1.31; 1.14–1.51) was linked to significantly increased risk of out-of-hospital cardiac arrest in following 30 days. This was not seen with naproxen, though few events occurred in this group.

An NHS choices assessment notes that the findings are limited by the following:

- Although the researchers used the same people to avoid confounding variables, the same person will differ in certain aspects over time.
- The study only looked at prescribed drugs and not over-the-counter drugs. In Denmark, ibuprofen was the only over-the-counter drug sold at the time of the study and therefore a large number of people taking ibuprofen might have been missed.
- People may have been taking NSAIDs for other underlying problems that increase the risk of cardiac arrest.

The dose and duration of NSAIDs might have varied across participants and it is not clear whether the greater the dose or duration, the higher the risk of cardiac arrest.

Deleted products 2016 | MIMS online for March 2016

Axorid (ketoprofen/omeprazole)	Gabup (buprenorphine)	Miacalcic (calcitonin [salmon])
Emeside (ethosuximide)	Isotrex (isotretinoin)	Zarontin (ethosuximide)

2. Drug safety update primarily relating to primary care prescribing

(For more information see Drug Safety Update) Volume 10 Issue 8 March 2016

Relevant to primary care

SGLT2 inhibitors: updated advice on increased risk of lower-limb amputation (mainly toes)

Update of previous advice published June 2016.

Canagliflozin may increase the risk of lower limb amputation (mainly toes) in patients with type 2 diabetes. Evidence does not show an increased risk for dapagliflozin and empagliflozin, but the risk may be a class effect.

The MHRA recommend that healthcare professionals should:

(a) Carefully monitor patients receiving canagliflozin who have risk factors for amputation, such as poor control of diabetes and problems with the heart and blood vessels.
(b) Consider stopping canagliflozin if patients develop foot complications such as infections, skin ulcers, osteomyelitis or gangrene.
(c) Advise patients receiving SGLT2 inhibitors about the importance of routine preventative foot care and adequate hydration.
(d) Continue to follow standard treatment guidelines for routine preventive foot care for people with diabetes.
(e) Report any suspected side effect with SGLT2 inhibitors on a yellow card.

Demeclocycline causing Acute Kidney Injury (AKI) – medication incident

There has been a serious incident within the region whereby a patient with normal renal function was prescribed oral Demeclocycline 300mg Three times a day, who then developed AKI one week after initiation. The patients U&Es had not been checked during the 7 days following initiation of treatment with this drug. Acute renal failure is documented as a side effect for Demeclocycline use in the BNF; however there is no indication of how often renal function should be specifically monitored in these patients.

Information & advice for prescribers in Primary Care:

(a) Demeclocycline is a **BROWN** drug & treatment should only be initiated by consultants/specialists. This drug should not be initiated by prescribers in primary care.
(b) Discharge/clinic letters from secondary care must contain clear information regarding the initiation, duration, monitoring and follow-up of treatment with Demeclocycline to enable prescribers to manage patients appropriately. Any ongoing monitoring / treatment should be discussed with the initiating consultant/specialist.
(c) Where prescribing by GPs has been requested after specialist initiation in secondary care, then this should only occur if there is a clearly documented plan under a hospital consultant specialist & what the monitoring requirements (especially renal function) are.

Gabapentinoids linked to heroin overdose deaths – use with caution in patients taking opioids

GPs should consider alternatives to the prescription drugs pregabalin and gabapentin, according to a new study that suggests a recent substantial increase in prescriptions is closely correlated with a rise in the number of overdose deaths in England and Wales. The use of gabapentinoids is especially dangerous when used with heroin or other opioids, as there is an increased risk of respiratory depression when used in combination. In cases where gabapentinoids are used in combination with opioids cannot be avoided, the dose of the gabapentinoid or opioids should be reduced appropriately and patients should be monitored for CNS depression, such as somnolence, sedation and respiratory depression.

Further information can be found at the following links:

(a) http://www.pulsetoday.co.uk/clinical/prescribing/gps-warned-as-gabapentinoids-is-linked-to-heroin-overdose-deaths/20034420.article
(b) http://onlinelibrary.wiley.com/doi/10.1111/add.13843/full

3. Local news and GP/pharmacist queries

Question: I wish to prescribe Sertraline for a patient with lactose intolerance. Which product shall I use?

Answer: Lactose is used widely in medicines as a diluent or filler in tablets, capsules, inhalers or liquids. Generally, the amount in medicines is very small. So, unless an adult has severe lactose intolerance, it would be unlikely to cause severe GI symptoms.

If lactose was to be avoided, the patient's community pharmacist can advise and dispense a suitable product.

Further information can be found at: https://www.sps.nhs.uk/articles/what-factors-need-to-be-considered-when-prescribing-for-lactose-intolerant-adults-2/

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

Highlighting potential QIPP opportunities:

Lidocaine 5% plasters

Drug tariff price (May 2017)

Preparation	Cost
Versatis	£72.40 x 30
Ralvo	£61.54 x 30

Epact data (Apr 16- Mar 17) for versatis

CCG	Items	Cost
SDCCG	897	£69,384
ECCG	385	£31,577
NDCCG	861	£62,537
HCCG	304	£23,573
Total	2447	£187,071

If the same number of items had been prescribed as Ralvo (instead of versatis) this could have potentially saved £36,483

Amoxil caps

Preparation	Cost	Preparation	Cost
Amoxil 250mg	92p x 21	Amoxicillin 250mg	£1.08 x 21
Amoxil 500mg	89p x 21	Amoxicillin 500mg	£1.29 x 21

Amoxil 250mg caps are **15% cheaper** than the generic amoxicillin 250mg caps (for a 7 day course), and amoxil 500mg caps are **31% cheaper** that the generic amoxicillin 500mg caps (for a 7 day course).

March

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	£16.50
Clindamycin 150mg capsules (new)	24	£4.17	£5.95
Dapsone 50mg tablets	28	£40.77	£46.19
Diamorpine 30mg powder for solution for injection ampoules (new)	5	£13.93	£16.52
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	30	£4.69	£7.76
Leflunomide 20mg tablets	30	£4.62	£8.90
Lorazepam 1mg tablets	28	£4.41	£6.00
Mirtazapine 15mg tablets	28	£1.19	£5.95
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	£11.20
Nitrofurantoin 50mg tablets	28	£11.66	£20.50
Oxazepam 10mg tablets	28	£1.37	£7.97
Oxazepam 15mg tablets	28	£1.38	£7.75
Ropinirole 1mg tablets	84	£2.07	£56.71
Ropinirole 2mg tablets	28	£2.80	£15
Ropinirole 5mg tablets	84	£3.91	£165.00
Spironolactone 50mg tablets	28	£1.70	£5.20
Valsartan 160mg capsules	28	£4.05	£17.65
Valsartan 40mg capsules	28	£3.31	£8.95
Valsartan 80mg capsules	28	£2.21	£11.99
Zolmitriptan 2.5mg tablets	6	£1.48	£15.30
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