

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.

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1. What's in the news

DTB select December 2016, Volume 54, Issue 12

Risk of heart failure with NSAIDs.

The cardiovascular effects of NSAIDs are well documented, with much of the evidence focused on thrombotic effects of selective and non-selective drugs.

Results from a large nested case-control study suggest that the risk of heart failure varies between individual NSAIDs and according to the dose used.

The study identified nearly 10 million adults starting NSAID treatment during 2000–2010. The study found that the risk of admission for heart failure increased with current use of seven traditional NSAIDs (diclofenac, ibuprofen, indometacin, ketorolac, naproxen, nimesulide and piroxicam) and two COX-2 inhibitors (etoricoxib and rofecoxib). Odds ratios ranged from 1.16 (95% CI 1.07 to 1.27) for naproxen to 1.83 (1.66 to 2.02) for ketorolac. The association with heart failure was confirmed regardless of whether there was recorded evidence of a previous diagnosis of heart failure. For most NSAIDs there was an increasing dose-dependent risk of heart failure hospitalisations. Celecoxib was not associated with a raised risk of hospital admissions for heart failure at commonly used doses. However, the authors could not rule out an association at very high doses.

Prescribers are reminded of the risk of admission for heart failure associated with commonly used NSAIDs. In general, NSAIDs should be avoided in people with heart failure or those at high risk of heart failure. If an NSAID is needed it should be used at the lowest possible dose for the shortest time and reviewed regularly. Locally we recommend ibuprofen initially 300-400mg 3-4 times daily, increase if necessary to max 2.4g daily, maintenance dose of 0.6-1.2g daily or naproxen 500mg to 1000mg daily in 1-2 divided doses; as first line treatment option for chronic non-malignant pain after careful assessment of the balance of benefits over the risks.

Update on the gliptins

DTB review looks at the evidence for clinical effectiveness and cardiovascular outcome studies for 3 gliptins – saxagliptin, linagliptin and alogliptin. (Previously sitagliptin and vildagliptin have been reviewed)

NICE NG28 recommends metformin as 1st line drug treatment for majority of type 2 diabetes patients. For control of HbA1c, dual therapy options include either addition of a gliptin, a sulfonylurea, a SGLT2i (flozin) or pioglitazone.

The DTB have reviewed the trials for saxagliptin, linagliptin and alogliptin, and all appear to provide similar, yet modest levels of HbA1c reduction of about 0.5-0.8% (approximately 5-9mmol/mol) when used over 6 months. These values are consistent with HbA1c reductions seen with the other 2 gliptins. Meta-analyses that compare gliptins with sulfonylurea and pioglitazone suggest at best equivalent HbA1c control and slightly improved weight profile, but treatment failure with gliptins was more common. Gliptins were associated with less hypoglycaemia than sulfonylurea.

In the cardiovascular outcome trials all 3 gliptins achieved non-inferiority for their composite primary cardiovascular safety endpoints but did not demonstrate long-term cardiovascular benefits. One trial reported an increased risk of hospitalisation for heart failure with saxagliptin.

Prescriber are reminded of the traffic light classification of gliptins - alogliptin GREEN first line, linagliptin GREEN alternative first line for patients with renal or hepatic impairment. Saxagliptin, sitagliptin and vildagliptin are BROWN with exceptionality due to intolerance to the preferred first line choices or restricted by their licensing. Alogliptin remains the cost effective gliptin of choice. When add on therapy is deemed appropriate, a gliptin should be considered for those patients where more cost-effective options e.g. a sulfonylurea are not suitable or where weight gain is likely to be a significant issue. Prescribers are reminded therapy with a gliptin (or gliptazone or SGLT2i) should only be continued if there is a reduction in HbA1c ≥ 5.5 mmol/mol (0.5%) in 6 months See local [type 2 diabetes guidance](#) for further details.

SMA Gold Prem 2	Calcium 500 (calcium carbonate)	Respontin (ipratropium bromide)
SMA Gold Prem 2 Liquid	Premique (conjugated oestrogens/medroxyprogesterone)	Tegretol suppositories (carbamazepine)

2. Drug safety update primarily relating to primary care prescribing
(For more information see [Drug Safety Update](#)) Volume 10 Issue 5 December 2016

Cobicisat, ritonavir and coadministration with a steroid: Clinicians who prescribe steroids to patients with HIV should be aware that concomitant use of a corticosteroid (including intranasal, inhaled and intra-articular preparations) and a HIV-treatment-boosting agent (ritonavir, cobicistat) may increase the risk of systemic corticosteroid adverse effect. If a corticosteroid is necessary (where the benefits outweigh the risk) then beclomethasone is the preferred corticosteroid. The safety highlights the importance of adding RED drugs onto clinical systems to help clinicians identify and avoid serious interactions.

Apremilast – new important advice regarding suicidal ideation and behaviour. Letter from Celgene sent to healthcare professional's highlights reports of suicidal ideation and behaviour from post marketing reports. Although apremilast is a RED drug, clinicians are advised to be aware of patients commenced this treatment by specialists and the importance of adding RED drugs onto clinical systems.

3. Local news and GP/pharmacist queries

Query from GP

What would be the best antidepressant for a patient with absence seizures?

Answer

This is a common query as patients with epilepsy are three times more likely to be prescribed an antidepressant than the general population and two times more likely to report suicidal thoughts. This may be explained by abnormalities in neurotransmitters which are common to both conditions. Antidepressants need careful consideration in patients with epilepsy due to their tendency to lower the seizure threshold and also due to interactions with some antiepileptic medications. The use of antidepressants in patients with epilepsy was considered in a UKMI Medicines Q&A, the key points being:

- The first consideration should always be to check the patient's anticonvulsant regimen for potential drug-induced depression. It may be that the patient would benefit from changing the anticonvulsant to another agent with a more favourable effect on mood rather than adding in an antidepressant. Changes to anticonvulsant medication should be made in consultation with the patient's specialist.
- The risk of seizures with most antidepressants is low, but is probably not zero for any of them, and patients should be made aware of this when prescribing. The risk of seizures increases with increasing doses.
- SSRIs are considered the first line antidepressant option in patients with epilepsy. Citalopram or sertraline may be considered the better options due to safety data and reduced interaction potential with the anticonvulsants. Fluoxetine is not the best choice due to its long half-life, a possibly greater incidence of seizures and an increased risk of drug interactions.
- Introducing the antidepressant gradually, starting with a low dose, and not exceeding the maximum recommended doses may reduce the risk of a seizure.
- If seizures occur or if the incidence of seizures increases, the antidepressant should be discontinued.

The full document can be found at <https://www.sps.nhs.uk/articles/what-is-the-most-appropriate-antidepressant-to-use-in-patients-with-epilepsy/>

CredibleMeds® Mobile Apps Available for QT Drugs Lists

This CredibleMeds Mobile App supports the CredibleMeds.org website which maintains and posts lists of drugs in categories that reflect their ability to prolong the QT interval on the electrocardiogram and/or cause the life-threatening heart arrhythmia, torsades de pointes (TdP). The CredibleMeds Mobile App was developed for patients with Congenital Long QT Syndrome, healthcare professionals and research scientists in order to provide them with ready access to the most up-to-date version of the CredibleMeds lists of drugs. The App also provides background information on the categories of drug risk and explains the relationship between QT prolongation and TdP.

You can access the iPhone application in the iOS App Store by clicking here: <https://itunes.apple.com/gb/app/crediblemeds-mobile/id1162818678?mt=8> Likewise, if you have an Android device, search the Google Play store for CredibleMeds or click the following: <https://play.google.com/store/apps/details?id=org.azcert.crediblemeds&rdid=org.azcert.crediblemeds>

Flu vaccines

Traffic light classification for the quadrivalent vaccines is as follows:

- **Fluenz Tetra nasal suspension: GREEN** - From Sept 2014 Fluenz Tetra is the preferred flu vaccine in all children aged 2, 3 and 4 year olds and in the at risk 5-17 year olds. The FLUENZ Tetra vaccine is available via IMMFORM made available through National Stock.
- **Fluarix Tetra pre-filled syringe: GREEN** - 2nd line to nasal preparations, as per national immunisation programme for children aged 3 upto 18 years.
- **Fluarix Tetra: BLACK** - For adults (aged 18 years and over)

Lost or stolen prescriptions

NHSE advice regarding [lost or stolen prescription](#) can be found on the Derbyshire Medicines Management website.

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

Highlighting expensive medicines

Doxepin - Drug tariff price (Jan 2017)

Strength	Cost
Doxepin 25mg caps	£110.34 x 28
Doxepin 50mg caps	£175.18 x 28

Epact data (Dec 15- Nov16) for all strengths:

BNF Name	Total Items	Cost
ECCG	20	£1,450
HCCG	115	£6,957
NDCCG	249	£36,576
SDCCG	263	£52,201
	647	£97,184

Patients on doxepin should be highlighted to the GP for review to switching to a cost effective alternative. Patients treated with doxepin for resistant depression should be reviewed at 12 and 24 months.

Dicycloverine – Drug tariff price (Jan 2017)

Strength	Cost
Dicycloverine 10mg tabs	£184.25 x 100
Dicycloverine 20mg tabs	£196.69 x 84

Epact data (Dec 15- Nov16) for all strengths

BNF Name	Total Items	Cost
ECCG	84	£17,545
HCCG	151	£22,991
NDCCG	747	£103,280
SDCCG	400	£69,236
	1,386	£213,065

Patients are most likely to be initiated by their GP. Specialists have recommended switch to mebeverine would be appropriate taking the patients clinical circumstances into account.

Price reduction

Tillotts Pharma UK Ltd has recently introduced a price reduction for Octasa MR. Prescribers are reminded that Octasa MR is the cost effective brand of choice for mesalazine MR

Product	Pack	NHS Tariff 2016	NHS Tariff 2017
Octasa 400	90	£ 19.50	£ 16.58
Octasa 400	120	£ 26.00	£ 22.10
Octasa 800	90	£ 47.50	£ 40.38
Octasa 800	180	£ 95.00	£ 80.75
Entocort 3mg	100	£ 99.00	£ 84.15
Entocort 20microgram/ml	7	£ 39.60	£ 33.66

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Note – The PSNC is still in discussion with the Department of Health on a number of generic medicines in short supply

Drug	Pack size	Current months Drug tariff price	Price concession
Amitriptyline 50mg tablets	28	£2.77	£3.05
Bumetanide 1mg tablets	28	£1.64	£1.75
Candesartan 2mg tablets	7	£1.92	£2.25
Dapsone 50mg tablets	28	£40.77	£46.19
Exemestane 25mg tablets	30	£5.71	£9.60
Flecainide 100mg tablets	60	£10.10	£13.60
Flecainide 50mg tablets	60	£8.64	£11.25
Fludroxycortide 4mcg/sq cm tape 7.5cm	20	£12.49	£12.49
Leflunomide 20mg tablets	30	£4.62	£10.99
Lorazepam 1mg tablets	28	£4.41	£6.05
Lorazepam 2.5mg tablets	28	£12.20	£12.50
Metronidazole 400mg tablets	21	£5.57	£7.88
Mirtazapine 15mg tablets	28	£1.19	£5.95

Mirtazapine 30mg tablets	28	£1.27	£1.55
Mirtazapine 45mg tablets	28	£1.55	£5.95
Naratriptan 2.5mg tablets	6	£4.21	£24.55
Nitrofurantoin 100mg tablets	28	£7.03	£14.05 ¹
Nitrofurantoin 50mg tablets	28	£11.66	£17.50
Quinagolide 75microgram tablets	30	£27	£49.50
Ropinirole 0.25mg tablets	12	£9.12	£5.70
Ropinirole 0.5mg tablets	28	£13.63	£18.15
Ropinirole 1mg tablets	84	£2.07	£56.71
Ropinirole 2mg tablets	28	£2.80	£31.51
Ropinirole 5mg tablets	84	£3.91	£165
Trospium Chloride 20mg tablets	60	£13.01	£15.47
Valsartan 160mg capsules	28	£4.05	£5.20
Valsartan 40mg capsules	28	£3.31	£4.17
Valsartan 80mg capsules	28	£2.21	£4.17
Zolmitriptan 2.5mg orodispersible tablets sugar free	6	£1.69	£23.99 ²
Zolmitriptan 2.5mg tablets	6	£1.48	£13.70

¹Nitrofurantoin MR 100mg BD is a cost-effective 1st line choice for empirical treatment of UTIs.

²Sumatriptan remains 1st line choice for the treatment of migraines.

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

NICE TA420 ticagrelor 60mg in combination with aspirin is recommended within its marketing authorisation as an option for preventing atherothrombotic events in adults who had a myocardial infarction and who are at high risk of a further event. Ticagrelor 60mg with aspirin is recommended as extended therapy (for up to 3 years) after the initial 12 month treatment with dual antiplatelet therapy.

Previously ticagrelor for the treatment of acute coronary syndrome (NICE TA236) was recommended at 90mg with aspirin for up to 12 months in adults with acute coronary syndrome to prevent further atherothrombotic events.

Ticagrelor has been classified as BROWN after specialist initiation. Local experts are reviewing the place of ticagrelor 60mg in current guidelines.

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