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 February 2016 Volume 54 issue 3

More doubts over nalmefene for alcohol dependence

A systematic literature review and meta-analysis has found little evidence to support the use of nalmefene in the treatment of alcohol dependence.

This is also covered previously in February's medicines management newsletter. The DTB similarly questions the use of nalmefene and could not recommend its use. DTB highlights the limitations of the evidence, the relatively modest reduction in drinking compared with placebo, lack of evidence on health-related outcomes and concerns over the generalisability of the data. Nalmefene has been locally classified as RED in line with NICE TA 325 and care under a specialist alongside behavioural interventions.

Nurse-led drug titration beneficial in heart failure

A Cochrane review of a Nurse-led titration of medicines to treat patients with heart failure can result in fewer hospital admissions and increased survival compared with titration by primary care physicians. The review did not explore the cost-effectiveness of nurse-led titration. This provides a valuable endorsement of the role of a nurse-led dose titration service showing an increase in survival and number of participants reaching target dose within a shorter time period.

Other news…

Effects of sodium-glucose cotransporter-2 (SGLT2) inhibitors on cardiovascular events, death, and major safety outcomes in adults with type 2 diabetes: a systematic review and meta-analysis

SGLT2 inhibitors are known to reduce glucose concentrations, blood pressure, and weight, but to increase LDL cholesterol and the incidence of urogenital infections

A systematic review and meta-analysis of 6 regulatory submissions found that sodium-glucose cotransporter-2 inhibitors reduced the risk of cardiovascular adverse events as well as cardiovascular death, heart failure and death from any cause. Data driven mainly from empagloflozin and the EMPA-REG OUTCOME trial. Adverse events were more difficult to quantify than was efficacy, with the effects of individual drugs in the class seeming to differ for some safety outcomes.

Our local type 2 diabetes guidance is being updated to reflect NICE NG28. This is a relatively new drug class (black triangle) and prescribers should be cautious in their use and report any adverse effects however minor to the MHRA.

http://www.thelancet.com/journals/landia/article/PIIS2213-8587(16)00052-8/abstract

The Use of Oral Anticoagulants for Stroke Prevention in Atrial Fibrillation Patients with History of Intra-Cranial Hemorrhage

The risk of further intra-cranial haemorrhage (ICH) and benefit of stroke risk reduction with the use of oral anticoagulants for patients with atrial fibrillation (AF) with a previous history of ICH remains unclear. Newer oral anticoagulants (NOACs) may be safer in relation to risk of ICH but patients with previous ICH were excluded from trials comparing NOACs with warfarin. Using the Health Insurance Research Database in Taiwan 12,917 patients with a history of ICH with a CHA2DS2-VASc score ≥2 was identified. These were divided into 3 groups, no treatment, anti-platelet therapy and warfarin.

The authors concluded that warfarin use may be beneficial for AF patients with prior ICH having a CHA2DS2-VASc score ≥6. Whether the use of non-vitamin K antagonist oral anticoagulants (NOACs) could lower the threshold for treatment deserves further study

CIRCULATIONAHA.115.019794 **Published online before print March 11, 2016, doi: 10.1161/CIRCULATIONAHA.115.019794**

Effectiveness of non-steroidal anti-inflammatory drugs for the treatment of pain in knee and hip osteoarthritis: a network meta-analysis

A network meta-analysis which included the Cochrane central register compared the interventions: NSAIDs, paracetamol, or placebo, for the treatment of osteoarthritis pain.

They concluded no role for single-agent paracetamol for the treatment of patients with osteoarthritis irrespective of dose. The effectiveness of NSAIDs varies substantially, with evidence of dose dependency. In view of the well-established harms of NSAIDs and the treatment duration in almost all the trials included in this analysis, intermittent short-term use of NSAIDs in moderate to maximum doses as required should be given preference over long-term fixed doses.

www.thelancet.com Published online March 17, 2016 http://dx.doi.org/10.1016/S0140-6736(16)30002-2

Deleted products 2016 | MIMS online for March 2016

Antabuse (disulfiram)	Dario Lancet	Dario Test Strip
FineTouch Test Tip	Medisafe Solo	Normax (co-danthrusate)
Perdix (moexipril)	Rapilysin (reteplase)	Unilet GP Superlite
Vexol (rimexolone)		

2. Drug safety update relating to primary care prescribing

(For more information see Drug Safety Update) Volume 9, Issue 8, March 2016

1. Trametinib (Mekinist▼): risk of gastrointestinal perforation and colitis
   Trametinib is authorised for unresectable or metastatic melanoma with a BRAF V600 mutation, either as monotherapy or in combination with dabrafenib
   Trametinib is locally classified as RED and should not be prescribed in primary care

Reminder- Letters sent to healthcare professionals in February 2016

2. In February 2016, a letter was sent to healthcare professionals regarding valproate, the risk of abnormal pregnancy outcomes and the new communication materials available (see also the associated Drug Safety Update article)

3. Local news and GP/pharmacist queries

Query from GP practice:

A GP has raised a query on the precise timing of gonadorelin analogues and what to do in the event of patients missing their clinic appointment.

Answer from a medicines management pharmacist:

The SPCs or product literature are a little unclear in that they do not distinguish whether administration is by calendar month defined by 28 days, 30 days or the exact calendar month. The trials to support the licensing imply a dosing of 28 days for the monthly injection.

There is little information on this from our main resources. The manufacturers were unable to comment about the minimum/maximum frequency between injections. However, the SPC states that "PROSTAP 3® provides continuous plasma levels for up to 117 days". This would suggest that in the majority of patients, if the injection was delayed by a week or so there would probably be no adverse effects in terms of treatment.

Consultant advice was sought:

Local consultant advice is that it takes six to 12 months for the testosterone to come back up so timing is not that critical. Up to a week after the scheduled appointment date would be acceptable.

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

Reminder

The place of liothyronine in the Derbyshire wide formulary is restricted to the following:

- Under the agreement of shared care for treatment resistant depression after specialist/consultant initiation
  - In combination with levothyroxine after consultant endocrinologists initiation.
    - A small number of patients may benefit from the addition of small doses of liothyronine in addition to levothyroxine if their quality of life remains poor despite adequate levothyroxine replacement (i.e. fT4 at upper limit or just over the upper limit of reference range) and where measured fT3 still in the lower half or lower than the lower limit of the reference range. In this situation after specialist Endocrinology advice, a clinical trial of at least 3 months may be worthwhile in order to ascertain whether this improves the patient's quality of life. If addition of liothyronine does not result in significantly improved symptoms after a three month trial then stop and resume levothyroxine monotherapy

Levothyroxine is the NHS thyroid hormone of choice as it is cost-effective, suitable for once daily dosing due to its long half-life and provides stable and physiological quantities of thyroid hormones for patients requiring replacement.

Liothyronine (available as licensed 20 microgram tablets and unlicensed 5 microgram tablets) is considerably more expensive than levothyroxine. Many other liothyronine-containing preparations (such as Armour Thyroid) are also unlicensed, therefore the safety and quality of these products cannot be assured.

Liothyronine is not routinely recommended for prescribing as it has a much shorter half-life and steady-state levels cannot be maintained with once daily dosing

Product	Cost per 28 tablets
Levothyroxine 25 microgram tablets	£3.11
Levothyroxine 50 microgram tablets	£2.12
Levothyroxine 100 microgram tablets	£2.11
Liothyronine 20 microgram tablets	£198.32
Other brands without a UK license ('specials')	£41 to £337 based on average cost per item (ePACT)

Primary care management of patients after weight loss surgery

This paper covers the common types of bariatric surgery covered by the NHS and how to manage obesity related comorbidities after surgery. It is usual that patients are usually followed up every two to three months for the first two years by the bariatric multidisciplinary team, then yearly by general practitioners in a shared care model (where primary care clinicians will need to liaise with the service). High level evidence for postoperative nutritional requirements and how should they be monitored is lacking. The British Obesity and Metabolic Surgery Society (BOMSS) has recently published recommendations based on observational data.

Recommended vitamin and mineral supplements after bariatric surgery161920

Supplement	Laparoscopic adjustable gastric banding	Roux-en-Y gastric bypass/laparoscopic sleeve gastrectomy
Multivitamin/ mineral*	Forceval one capsule daily OR one over the counter complete multivitamin and mineral supplement daily	Forceval one capsule daily OR two over the counter complete multivitamin and mineral supplements daily
Iron	No supplement given routinely	200 mg ferrous sulphate daily
Folic acid	No supplement given routinely	No supplement needed unless deficient
Vitamin B12†	No supplement given routinely	Three monthly intramuscular injection of 1 mg hydroxocobalamin
Calcium + vitamin D	No supplement given routinely	Continue with maintenance dose identified preoperatively. Likely to be at least 800 mg calcium + 20µg vitamin D (eg, Accrete D3)

*For bypass and sleeve gastrectomy, supplements should contain a minimum of 2 mg copper/day. Forceval contains 2 mg; however, most over the counter products such as Sanatogen A-Z contain only 1 mg of copper, so two tablets/day will be needed.

†Three monthly intramuscular vitamin B12 injections are recommended for all patients who have bypass or sleeve gastrectomy owing to frequency with which vitamin B12 deficiency occurs.

It is recognised also that patients need careful biochemical monitoring, depending on the type of procedure.

Guidance for Annual blood tests following bariatric surgery can also be found on the BOMMS website
For more information see http://www.bomss.org.uk/nutritional-guidelines/

BMJ 2016;352:i945 doi: 10.1136/bmj.i945 (Published 10 March 2016)

Local guidance to support Primary Care prescribers is in development

Generic shortages (NCSO and price concessions)

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.

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Drug	Pack size	Drug tariff price	Price concession
Bumetanide 1mg tablets	28	£1.30	£2.05
Celiprolol 400mg tablets	28	£32.32	£39.65
Cimetidine 400mg tablets	60	£9.72	£19.99
Desmopressin 10micrograms/dose nasal spray (new)	60 dose	£13.77	£24.00
Flecainide 50mg tablets	60	£3.35	£7.50
Flecainide 100mg tablets	60	£4.32	£6.83
Fludrocortisone 100mcg tablets (new)	100	£5.05	£96.00
Lamotrigine 5mg dispersible tablets sugar free	28	£2.68	£7.50
Mefenamic acid 500mg tablets	28	£8.25	£10.25
Nitrofurantoin 100mg tablets (new)	28	£2.88	£12.50
Nitrofurantoin 50mg tablets (new)	28	£8.23	£11.50
Pioglitazone 15mg tablets	28	£11.23	£19.20
Pioglitazone 30mg tablets	28	£10.99	£24.32

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

Nothing 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