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.4 April 2017

Bazedoxifene for HRT

Duavive is a modified release formulation of conjugated oestrogens plus bazedoxifene acetate. It is licenced for oestrogen deficiency symptoms in postmenopausal women with a uterus at least 1 year after last menses, when progestogen-containing therapy is inappropriate. Launched in UK in July 2016. DTB present a review of the evidence on efficacy and safety.

Clinical trials have shown that conjugated oestrogens/bazedoxifene produced a modest reduction in the number of moderate and severe hot flushes, and improvements in measures of quality of life and sleep in younger postmenopausal women for periods of up to two years. However, the majority of the evidence comes from a single series of clinical studies with no direct comparisons with conventional HRT.

The combination of oestrogen with a selective oestrogen receptor modulator holds the possibility of HRT without the concerns of breast cancer. There remains some uncertainty relating to endometrial safety during long-term treatment. We believe that independent confirmation of efficacy and safety, direct comparisons with conventional HRT, and more experience in older women and for longer periods will be needed before it can be recommended as an alternative to standard HRT products

JAPC have classified conjugated oestrogens & bazedoxifene acetate (Duavive) as BLACK (not routinely recommended or commissioned), based on lack of data on safety compared with standard therapy

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Lidocaine/prilocaine spray for premature ejaculation

A new formulation (cutaneous spray) was launched in the UK November 2016 for the treatment of primary premature ejaculation. DTB present a review of the evidence for efficacy and safety.

Lidocaine/prilocaine spray (150mg/mL and 50mg/mL, respectively) is licensed for the topical treatment of primary premature ejaculation. A few short-term studies funded by the company have shown that in heterosexual men with stable relationships there was a mean increase in ejaculatory latency of 2–3 minutes compared with placebo spray. Men with erectile dysfunction were excluded from these trials, although erectile dysfunction and premature ejaculation often co-exist. We found no published studies that compared lidocaine/prilocaine spray with alternative active treatments. Unwanted effects include erectile dysfunction and genital hypoaesthesia among men, and vulvovaginal burning sensation, discomfort, pain or pruritus in their partners. In addition, the product is noted to reduce the strength of polyurethane condoms. Long-term benefits or harms are unknown. Although lidocaine/prilocaine spray is available via a private prescription and costs £100 for a device that will deliver 20 doses, its status within NHS prescribing needs clarifying. As it is considerably more expensive than off-label use of a SSRI or lidocaine/prilocaine cream, we do not recommend lidocaine/prilocaine topical spray as first-line therapy.

JAPC have classified Lidocaine/Prilocaine (Fortacin) as BLACK (not routinely recommended or commissioned).

Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD012066. DOI: 10.1002/14651858.CD012066.pub2.

LABA/LAMA for COPD treatment.

Long-acting muscarinic antagonist (LAMA) plus long-acting beta-agonist (LABA) versus LABA plus inhaled corticosteroid (ICS) for stable chronic obstructive pulmonary disease (COPD)

The systematic review (n=9,839) compared the benefits and harms of LAMA/LABA versus LABA/ICS for treatment of people with stable COPD. The review suggests LABA/LAMA combinations are linked to fewer exacerbations, larger improvement of FEV1, lower risk of pneumonia and more frequent improvement in quality of life in patients with moderate to severe disease than LABA/ICS.

The review adds to the growing body of evidence of use of LABA/LAMA combinations over LABA/ICS for patients with FEV1<50%. The LABA/LAMA combination has added benefit of steroid-sparing side-effects. Locally the COPD guidance has been updated to include the LAAB/LAMA combination for patient with FEV1<50%.

DTB, vol55, no.4. April 2017

Screen and treat approaches for diabetes prevention

A systematic review and meta-analysis of screening tests and interventions found that screen and treat policies, employed in isolation are unlikely to significantly impact upon the burden of type 2 diabetes. The review is the first to assess both the diagnostic accuracy of screening tests for pre-diabetes and the efficacy of interventions in those detected through screening. The investigators searched for studies of diagnostic accuracy and prevalence, focusing on laboratory assessed HbA1c and fasting plasma glucose as screening tools.

The review has highlighted many of the uncertainties associated with defining, identifying and managing people at high risk of developing diabetes using a screen and test approach. It is important that such limitations are taken into account, particularly as there is growing interest in drug treatment for high risk patients. While lifestyle interventions are unlikely to cause significant harm, greater use of drug therapy to delay the onset of diabetes will expose large numbers of people to potential adverse effects.

Deleted products 2017 | MIMS online for April 2017

Ebesque XL (quetiapine)	Distamine (penicillamine)	Isopto Alkaline (hypromellose)
Kemicetine (chloramphenicol)	Macugen (pegaptanib)	Tobravisc (tobramycin)

2. Drug safety update primarily relating to primary care prescribing

(For more information see Drug Safety Update) Volume 10 Issue 9 April 2017

Relevant to primary care

Valproate and neurodevelopmental disorders: new alert asking for patient review and further consideration of risk minimisation.

Patient safety alert has been issued asking all organisations to undertake systematic identification of women and girls taking valproate.

Advice for healthcare professionals:

- Do not prescribe valproate medicines for epilepsy or bipolar disorder in women and girls unless other treatments are ineffective or not tolerated migraine is not a licensed indication.
- Ensure women and girls taking valproate medicines understand the 30-40% risk of neurodevelopmental disorders and 10% risk of birth defects and are using effective contraception.
- Valproate use in women and girls of childbearing potential must be initiated and supervised by specialists in the treatment of epilepsy or bipolar disorder.

Patient Safety Alert - Resources to support the safety of girls and women who are being treated with valproate

The MHRA and NHS Improvement have also jointly published a Patient Safety Alert on 6th April 2017 highlighting resources to support the safety of girls and women who are being treated with valproate. This includes actions for GP practices and Community Pharmacies as follows:

(a) Identify how the resources signposted in this alert can be used to support fully informed decisions on the use of valproate by girls and women of childbearing age.

(b) Develop an action plan to ensure all girls and women of or nearing childbearing age taking valproate are systematically identified so that all relevant resources can be used to plan their care.

(c) Ensure relevant resources are embedded in clinical practice for current and future patients by revising local training, procedures and protocols.

(d) By circulating this Alert or through local alternatives (such as newsletters and local awareness campaigns) ensure staff are aware of the MHRA resources and understand their role in local plans to identify all girls and women of childbearing age taking valproate.

*Community pharmacies should deliver all actions that are within their remit, but systematic identification will typically need to be undertaken by the organisation prescribing valproate.

3. Local news and GP/pharmacist queries

QUESTION: GP is requesting information on magnesium replacement.

ANSWER: There are no national guidelines for the treatment of acute hypomagnesaemia, and practice varies widely across hospital Trusts.

Locally Derby hospital has produced some helpful guidance http://www.derbyhospitals.nhs.uk/primary/pathology/shared-care-pathology-guidelines/

Definition : Magnesium < 0.70 mmol/L

When is hypomagnesaemia considered a medical emergency?

- Magnesium 0.50 – 0.70 mmol/L - Not a medical emergency
- Magnesium 0.30 – 0.50 mmol/L - Possible medical emergency
- Magnesium <0.30 mmol/L - May be medical emergency

For unknown causes of severe hypomagnesaemia (<0.50 mmol/L), consider referral to hospital dependent upon symptoms and other results.

- If asymptomatic, immediate referral is not required. Consider oral replacement (as below) and referral to appropriate specialty dependent on the patient's history. Endocrine advice is available by choosing 'Advice and Guidance' from NHS e-Referrals

Oral administration

This is used for chronic magnesium loss or moderately severe hypomagnesaemia i.e. where there is a serum magnesium level of approximately 0.4 - 0.7mmol/L and patients are asymptomatic. Give up to 50 mmol day.

Suggested initial treatment is;

- **Maalox 10-20 ml qds (10ml Maalox = 6.8mmol Mg)**

During oral replacement monitor response by rechecking magnesium 1-2 weekly initially depending on clinical context. Reversal of hypomagnesaemia with oral replacement may take 6-8 weeks. Long term maintenance replacement may be needed if a reversible cause is not found and removed. In these circumstances, aim to maintain normal serum magnesium using the lowest effective dose of oral replacement. Long term maintenance may be required if cause is not found and corrected, but consider hospital referral if cause is unknown.

Diarrhoea tends to limit the amount of magnesium that can be given orally; if diarrhoea develops reduce the dose. The aluminium contained in Maalox may reduce the chance of diarrhoea.

See the guidance for more information on potential causes and stopping PPIs if appropriate. If the patient is symptomatic consider emergency referral.

What patient should do if they miss a dose of their medicine?

Specialist Pharmacy Service has produced a document regarding what patient should do if they miss a dose of their medicine.

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

Highlighting potential QIPP opportunities:

Alzest patches

Strength	Alzest patches	Rivastigmine patches
4.6mg/24 hour patch	£35.10 x 30	£77.97 x 30
9.5mg/24 hour patch	£19.97 x 30	£30.02 x 30
13.3mg/24 hour patch	[redacted]	£77.97 x 30

(MIMs online June 2017)

ePACT (Apr 16 – Mar 17) for Rivastigmine patches

SDCCG	4.6mg/24hrs	697	£48,707	9.5mg/24hrs	1,933	£49,896
ECCG	4.6mg/24hrs	102	£7,800	9.5mg/24hrs	202	£4,934
NDCCG	4.6mg/24hrs	397	£30,383	9.5mg/24hrs	419	£9,418
HCCG	4.6mg/24hrs	88	£5,950	9.5mg/24hrs	90	£2,369
		697	***£48,707***		***2,644***	***£66,617***

If the same number of items for 4.6mg/24hr patch had been prescribed as Alzest (instead of Rivastigmine) this could have potentially saved £24,242

If the same number of items for 9.5mg/24hr patch had been prescribed as Alzest (instead of Rivastigmine) this could have potentially saved £13,816

April

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	£3.00	£3.50
Buspirone 5mg tablets	30	£6.97	£16.50
Busipirone 10mg tablets	30	£3.81	£9.57
Clindamycin 150mg capsules	24	£4.17	£5.95
Dapsone 50mg tablets	28	£41.37	£46.19
Diamorpine30mg pwder for solution for injection ampoules	5	£13.93	£16.52
Ethosuximide 250mg.5ml oral solution	200ml	£4.22	£173.00
Exemestane 25mg tablets	30	£8.00	£11.50
Flecainide 100mg tablets	60	£12.14	£16.53
Flecainide 50mg tablets	60	£10.00	£11.57
Glibenclamide 5mg tablets	28	£2.32	£2.49
Leflunomide 10mg tablets	30	£5.24	£7.76
Leflunomide 20mg tablets	30	£7.66	£8.90
Lorazepam 1mg tablets	28	£5.26	£6.00
Mirtazapine 15mg tablets	28	£2.31	£3.00
Mirtazapine 30mg tablets	28	£1.25	£1.40
Mirtazapine 45mg tablets	28	£2.60	£3.00
Naratriptan 2.5mg tablets	6	£23.13	£23.00
Nitrofurantoin 100mg tablets	28	£9.85	£11.20
Nitrofurantoin 50mg tablets	28	£14.95	£20.50
Oxazepam 10mg tablets	28	£3.63	£7.97
Oxazepam 15mg tablets	28	£2.72	£7.97
Pramipexole 88microgram tablets	30	£1.39	£8.50
Ropinirole 1mg tablets	84	£56.71	£56.71
Ropinirole 2mg tablets	28	£38.74	£15
Ropinirole 5mg tablets	84	£3.98	£165.00
Spironolactone 50mg tablets	28	£3.16	£5.20
Valsartan 160mg capsules	28	£4.78	£17.25
Valsartan 40mg capsules	28	£3.44	£8.95
Valsartan 80mg capsules	28	£3.63	£11.50
Zolmitriptan 2.5mg tablets	6	£5.06	£15.30
Zolmitriptan 2.5mg oradispersible 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